STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 130901

TO: Zohreh Fay **Location: 3a61 / 3c70** **Wednesday, September 01, 2004** **Art Unit: 1614** **Phone: 272-0573** **Serial Number: 10 / 606501**	**From: Jan Delaval** **Location: Biotech-Chem Library** **Rem 1A51** **Phone: 272-2504** **jan.delaval@uspto.gov**

Search Notes

130901

Access DB# _____

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Johnie h Fay Examiner #: 66646 Date: 8/26/04
Art Unit: 1614 Phone Number 30(571) 272 0573 Serial Number: 10/606,501
Mail Box and Bldg Room Location: Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: use of Panecortave Acetate for the protection of visual Acuity in patients with Age related Macular Degeneratic

Inventors (please provide full names): _____

Earliest Priority Filing Date: 8/5/02

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

please search the claimed ~~method of~~ composition and method of use.

Jan

****

STAFF USE ONLY

	Type of Search	Vendors and cost where applicable
Searcher: Jan	NA Sequence (#)	STN ✓
Searcher Phone #: 22504	AA Sequence (#)	Dialog
Searcher Location	Structure (#)	Questel/Orbit
Date Searcher Picked Up: 9/1	Bibliographic ✓	Dr.Link
Date Completed: 9/1	Litigation	Lexis/Nexis
Searcher Prep & Review Time:	Fulltext	Sequence Systems
Clerical Prep Time: 10	Patent Family	WWW/Internet
Online Time: 35	Other	Other (specify)

PTO-1590-8 (01)

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=> fil reg
FILE 'REGISTRY' ENTERED AT 16:23:44 ON 01 SEP 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file
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STRUCTURE FILE UPDATES:   31 AUG 2004  HIGHEST RN 736193-62-7
DICTIONARY FILE UPDATES:  31 AUG 2004  HIGHEST RN 736193-62-7

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d ide can l1

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   7753-60-8  REGISTRY
CN   Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI)  (CA
     INDEX NAME)
OTHER CA INDEX NAMES:
CN   Pregna-4,9(11)-diene-3,20-dione, 17,21-dihydroxy-, 21-acetate (6CI, 7CI,
     8CI)
OTHER NAMES:
CN   21-Acetoxypregna-4,9(11)-dien-17α-ol-3,20-dione
CN   Al 3789
CN   Anecortave
CN   Anecortave acetate
CN   NSC 15475
CN   NSC 24345
FS   STEREOSEARCH
MF   C23 H30 O5
LC   STN Files:   ADISINSIGHT, ADISNEWS, BEILSTEIN*, BIOSIS, BIOTECHNO, CA,
       CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CIN, EMBASE, IFICDB,
       IFIPAT, IFIUDB, IMSDRUGNEWS, IMSRESEARCH, IPA, MRCK*, PHAR, PROMT,
       PROUSDDR, PS, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:   EINECS**
         (**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA  CAplus document type:  Dissertation; Journal; Patent
RL.P   Roles from patents:  BIOL (Biological study); PREP (Preparation); PROC
       (Process); RACT (Reactant or reagent); USES (Uses); NORL (No role in
       record)
RL.NP  Roles from non-patents:  BIOL (Biological study); PREP (Preparation);
       PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES
       (Uses); NORL (No role in record)

Absolute stereochemistry.
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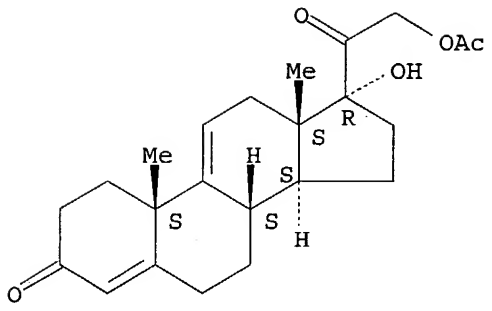


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

89 REFERENCES IN FILE CA (1907 TO DATE)
89 REFERENCES IN FILE CAPLUS (1907 TO DATE)
27 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 140:297513

REFERENCE 2: 140:157931

REFERENCE 3: 140:26949

REFERENCE 4: 139:265771

REFERENCE 5: 139:97753

REFERENCE 6: 139:53197

REFERENCE 7: 137:10999

REFERENCE 8: 134:91141

REFERENCE 9: 132:31278

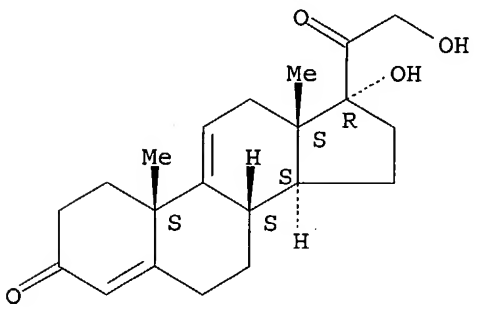
REFERENCE 10: 132:520

=> d ide can 19

L9 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN **10184-70-0** REGISTRY
CN Pregna-4,9(11)-diene-3,20-dione, 17,21-dihydroxy- (7CI, 8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN 17,21-Dihydroxypregna-4,9(11)-diene-3,20-dione
CN AL 4940
FS STEREOSEARCH
MF C21 H28 O4
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, IFICDB, IFIPAT, IFIUDB, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); RACT (Reactant or reagent)
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation);

PROC (Process); PRP (Properties); USES (Uses); NORL (No role in record)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

45 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
45 REFERENCES IN FILE CAPLUS (1907 TO DATE)
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 140:157931

REFERENCE 2: 140:26949

REFERENCE 3: 139:97753

REFERENCE 4: 138:170402

REFERENCE 5: 132:31278

REFERENCE 6: 132:520

REFERENCE 7: 131:351535

REFERENCE 8: 131:54038

REFERENCE 9: 128:39554

REFERENCE 10: 120:164649

=> d his

(FILE 'HOME' ENTERED AT 16:07:03 ON 01 SEP 2004)
SET COST OFF

FILE 'REGISTRY' ENTERED AT 16:07:11 ON 01 SEP 2004
E ANECORTAVE/CN
L1 1 S E3,E4
SEL RN
L2 0 S E1/CRN

FILE 'HCAPLUS' ENTERED AT 16:08:35 ON 01 SEP 2004
L3 89 S L1
L4 10 S ANECORTAVE OR ANECORTAVE ACETATE OR NSC15475 OR NSC24345 OR N
L5 91 S L3,L4

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L6           14 S L5 AND (EYE+OLD,NT,PFT,RT OR EYE, DISEASE+OLD,NT,PFT,RT)/CT
L7            9 S L5 AND EYE#/CW (L) DISEASE
L8           14 S L6,L7

     FILE 'REGISTRY' ENTERED AT 16:11:26 ON 01 SEP 2004
L9            1 S 10184-70-0
L10           0 S 10184-70-0/CRN

     FILE 'HCAPLUS' ENTERED AT 16:11:47 ON 01 SEP 2004
L11          45 S L9
L12           1 S AL4940 OR AL 4940
L13          45 S L11,L12
L14           8 S L13 AND (EYE+OLD,NT,PFT,RT OR EYE, DISEASE+OLD,NT,PFT,RT)/CT
L15           6 S L13 AND EYE#/CW (L) DISEASE
L16          16 S L8,L14,L15
L17         119 S L5,L13
L18           0 S L17 AND AMD
L19           3 S L17 AND MACUL? DEGENER?
L20           3 S L17 AND EYE, DISEASE/CT (L) (MACULA OR DEGEN? OR SENIL?)
L21          16 S L16,L19-L20
L22          13 S L21 NOT L19,L20
                E EYE+ALL/CT
L23      184018 S E26+OLD,NT,PFT,RT OR E27+OLD,NT,PFT,RT OR E28+OLD,NT,PFT,RT
L24          11 S L17 AND L23
L25           3 S L24 AND L19,L20
L26           8 S L24 NOT L25
L27          13 S L22,L26
L28           1 S US20040127472/PN OR (WO2003-US20154 OR US2002-401220#)/AP,PRN
                E JERDAN J/AU
L29           7 S E4-E6
                E ZILLIOX P/AU
L30           2 S E4
                E ROBERTSON S/AU
L31         151 S E3,E15,E16
                E ROBERTSON STELLA/AU
L32          20 S E3-E5
L33           2 S L17 AND L28-L32
                E ALCO/PA,CS
                E ALCOM/PA,CS
L34         877 S E3-E8 OR ALCON?/PA,CS
L35          12 S L17 AND L34
L36          19 S L19-L22,L27,L28,L35
L37          19 S L36 AND L3-L8,L11-L36
L38          18 S L37 AND (PD<=20020805 OR PRD<=20020805 OR AD<=20020805)
L39           2 S L19,L20 AND L38
L40           3 S L19,L20,L39
L41          16 S L37-L38 NOT L40
                SEL DN AN 15 16
L42          14 S L41 NOT E1-E6
L43           1 S L33,L35 NOT L40,L42
L44          16 S L41,L42

     FILE 'REGISTRY' ENTERED AT 16:23:44 ON 01 SEP 2004

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 16:23:57 ON 01 SEP 2004
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FILE COVERS 1907 - 1 Sep 2004 VOL 141 ISS 10
FILE LAST UPDATED: 31 Aug 2004 (20040831/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d l44 all hitstr tot

L44 ANSWER 1 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:428756 HCAPLUS
DN 137:10999
ED Entered STN: 07 Jun 2002
TI Methods for reducing or preventing transplant rejection in the eye and intraocular implants for use therefor
IN Wong, Vernon G.
PA Oculex Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61L027-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002043785	A2	20020606	WO 2001-US44481	20011128 <--
	WO 2002043785	A3	20021121		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002036495	A5	20020611	AU 2002-36495	20011128 <--
	US 2002182185	A1	20021205	US 2001-997094	20011128 <--
	US 6699493	B2	20040302		
	EP 1339438	A2	20030903	EP 2001-986027	20011128 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001015772	A	20040113	BR 2001-15772	20011128 <--
	JP 2004514702	T2	20040520	JP 2002-545755	20011128 <--
	US 2004137034	A1	20040715	US 2003-744560	20031222 <--
	JP 2004210798	A2	20040729	JP 2004-121618	20040416 <--
PRAI	US 2000-250023P	P	20001129 <--		
	US 2001-298253P	P	20010612 <--		
	JP 2002-545755	A3	20011128 <--		
	US 2001-997094	A1	20011128 <--		
	WO 2001-US44481	W	20011128 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES

WO 2002043785	ICM	A61L027-00
US 2002182185	ECLA	A61K009/00M16B <--
JP 2004514702	FTERM	4C076/AA51; 4C076/AA95; 4C076/BB24; 4C076/BB32; 4C076/CC07; 4C076/EE24A; 4C076/EE24M; 4C076/EE32A; 4C076/EE32M; 4C076/FF32; 4C084/AA02; 4C084/AA17; 4C084/BA44; 4C084/DA11; 4C084/MA02; 4C084/MA36; 4C084/MA58; 4C084/MA67; 4C084/NA10; 4C084/NA12; 4C084/ZB082; 4C084/ZC082; 4C086/AA01; 4C086/AA02; 4C086/DA10; 4C086/MA02; 4C086/MA03; 4C086/MA05; 4C086/MA07; 4C086/MA36; 4C086/MA58; 4C086/MA67; 4C086/NA10; 4C086/NA12; 4C086/ZB08 <--
JP 2004210798	FTERM	4C076/AA67; 4C076/AA94; 4C076/BB24; 4C076/CC10; 4C076/CC29; 4C076/EE24A; 4C076/FF31; 4C086/AA01; 4C086/AA02; 4C086/DA10; 4C086/MA02; 4C086/MA05; 4C086/MA58; 4C086/NA12; 4C086/ZA33; 4C086/ZB21 <--

AB Methods for reducing or preventing transplant rejection in the eye of an individual are described, comprising: (a) performing an ocular transplant procedure; and (b) implanting in the eye a bioerodible drug delivery system comprising an immunosuppressive agent and a bioerodible polymer. Sustained-release intraocular implant containing HPMC 15, PLGA 35, and dexamethasone 50% were prepared The implants were implanted in the anterior chamber of the rat eyes at the end of cornea transplants surgery. Rats did not show any sign of rejection and the corneas stayed clear in all eyes. After 8 wk the graft survival was 100%.

ST transplant rejection eye intraocular implant; intraocular implant PLGA dexamethasone transplant rejection

IT **Eye**
(anterior chamber; methods for reducing or preventing transplant rejection in eye and intraocular implants for use therefor)

IT Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bioerodible; methods for reducing or preventing transplant rejection in eye and intraocular implants for use therefor)

IT **Eye**
(cornea, transplant; methods for reducing or preventing transplant rejection in eye and intraocular implants for use therefor)

IT Transplant and Transplantation
(cornea; methods for reducing or preventing transplant rejection in eye and intraocular implants for use therefor)

IT Human
Immunosuppressants
Transplant rejection
(methods for reducing or preventing transplant rejection in eye and intraocular implants for use therefor)

IT Polyesters, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for reducing or preventing transplant rejection in eye and intraocular implants for use therefor)

IT **Eye**
(pigment epithelium, transplant; methods for reducing or preventing transplant rejection in eye and intraocular implants for use therefor)

IT **Intraocular lenses**
(sustained-release; methods for reducing or preventing transplant rejection in eye and intraocular implants for use therefor)

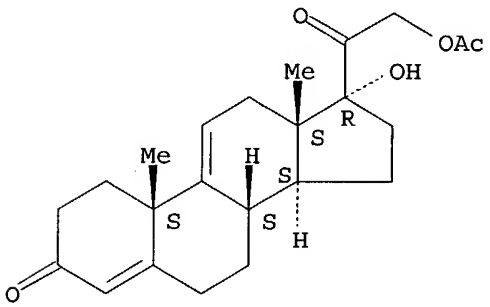
IT 50-02-2, Dexamethasone 50-24-8, Prednisolone 50-44-2, 6-Mercaptopurine 50-91-9, Floxuridine 51-21-8, Fluorouracil 54-25-1, 6-Azauridine 59-05-2, Methotrexate 89-38-3, Pteropterin 124-94-7, Triamcinolone 147-94-4, Cytarabine 154-42-7, Thioguanine 320-67-2, Azacitidine 426-13-1, Fluorometholone 446-86-6, Azathioprin 807-38-5, Fluocinolone 2668-66-8, Medrysone 3094-09-5, Doxifluridine 4291-63-8, Cladribine 5581-52-2, Thiamiprine **7753-60-8**, **Anecortave**

acetate 9004-65-3, Hydroxypropyl methylcellulose 17902-23-7, Tegafur 21679-14-1, Fludarabine 22006-84-4, Denopterin 31698-14-3, Ancitabine 34346-01-5, Glycolic acid lactic acid copolymer 50924-49-7, Mizoribine 52128-35-5, Trimetrexate 55726-47-1, Enocitabine 59865-13-3, Cyclosporin a 61422-45-5, Carmofur 72732-56-0, Piritrexim 80576-83-6, Edatrexate 95058-81-4, Gemcitabine 96187-53-0, Brequinar 98629-43-7, Gusperimus 104987-11-3, Tacrolimus 110690-43-2, Emitefur 112887-68-0, Tomudex
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for reducing or preventing transplant rejection in eye and intraocular implants for use therefor)

IT **7753-60-8, Anecortave acetate**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for reducing or preventing transplant rejection in eye and intraocular implants for use therefor)

RN 7753-60-8 HCAPLUS
CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 2 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:25776 HCAPLUS
DN 134:91141
ED Entered STN: 11 Jan 2001
TI Combination therapy for lowering and controlling intraocular pressure containing angiostatic steroids
IN Clark, Abbot F.
PA **Alcon Laboratories, Inc., USA**
SO U.S., 7 pp.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-56
NCL 514179000
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 6172054	B1	20010109	US 1995-491005	19950615 <--
PRAI US 1995-491005		19950615 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 6172054	ICM	A61K031-56
	NCL	514179000

OS MARPAT 134:91141

AB Angiostatic agents and another IOP lowering compound are combined in ophthalmic compns. to treat glaucoma and ocular hypertension. Methods for treating glaucoma and ocular hypertension are also disclosed. A solution was prepared contg timolol maleate and 4,9(11)-pregnadiene-17α,21-diol-3,20-dione 21 acetate.

ST glaucoma therapy angiostatic steroid; intraocular pressure angiostatic steroid compn

IT Adrenoceptor agonists
Angiogenesis
Antiglaucoma agents
(combination therapy for lowering and controlling intraocular pressure containing angiostatic steroids)

IT Prostaglandins
Steroids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy for lowering and controlling intraocular pressure containing angiostatic steroids)

IT Drug delivery systems
(solns., ophthalmic; combination therapy for lowering and controlling intraocular pressure containing angiostatic steroids)

IT Adrenoceptor antagonists
(β-; combination therapy for lowering and controlling intraocular pressure containing angiostatic steroids)

IT 53-02-1, Tetrahydrocortisol 57-63-6, 17α-Ethynylestradiol **7753-60-8** 26839-75-8, Timolol 26921-17-5, Timolol maleate 63659-18-7, Betaxolol 63659-19-8, Betaxolol hydrochloride 73218-79-8, Apraclonidine hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy for lowering and controlling intraocular pressure containing angiostatic steroids)

IT 9001-03-0, Carbonic anhydrase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; combination therapy for lowering and controlling intraocular pressure containing angiostatic steroids)

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

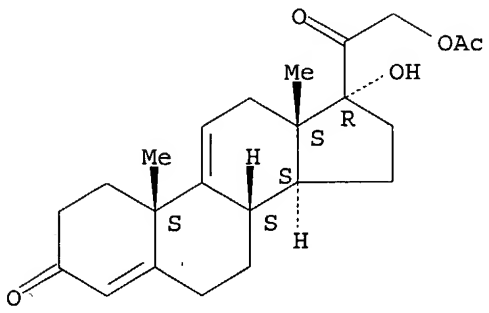
(1) Baldwin; US 4797413 1989 HCAPLUS
(2) Bito; US 4599353 1986 HCAPLUS
(3) Bondi; US 4730013 1988 HCAPLUS
(4) Clark; US 4876250 1989 HCAPLUS
(5) Clark; US 5371078 1994 HCAPLUS
(6) Clark; IOVS 1994, V35(Suppl), P1057
(7) Dean; US 5153192 1992 HCAPLUS
(8) Dean; US 5240923 1993 HCAPLUS
(9) Dean; US 5378703 1995 HCAPLUS
(10) Ingber; Endocrinology 1986, V119, P1768 HCAPLUS
(11) Jani; US 4911920 1990 HCAPLUS
(12) Johnson; Mayo Clin Proc, Glaucoma:An Overview 1986, V61, P59 MEDLINE
(13) Knepper; Pediat Neurosci 1985, V12, P240 HCAPLUS
(14) Lang; US 5403841 1995 HCAPLUS
(15) Lloyd; US 4540408 1985
(16) Mazuel; US 4861760 1989 HCAPLUS
(17) Missel; US 5212162 1993 HCAPLUS
(18) Rohen; Ophthalmology 1983, V90(7) MEDLINE
(19) Stjernschantz; US 5321128 1994 HCAPLUS
(20) Woodward; US 5093329 1992 HCAPLUS

IT **7753-60-8**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy for lowering and controlling intraocular pressure containing angiostatic steroids)

RN 7753-60-8 HCAPLUS

CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 3 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:10622 HCAPLUS
DN 132:31278
ED Entered STN: 06 Jan 2000
TI Angiostatic steroids
IN Clark, Abbot F.; Conrow, Raymond E.
PA **Alcon Laboratories, Inc., USA**
SO U.S., 18 pp.
CODEN: USXXAM
DT Patent
LA English
IC ICM A01N045-00
ICS C07J053-00; C07J005-00; C07J007-00
NCL 514171000
CC 2-4 (Mammalian Hormones)
Section cross-reference(s): 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 6011023	A	20000104	US 1997-924419	19970827 <--
PRAI US 1997-924419		19970827 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 6011023	ICM	A01N045-00
	ICS	C07J053-00; C07J005-00; C07J007-00
	NCL	514171000

AB Methods and compns. for preventing and treating neovascularization with angiostatic steroids is disclosed.
ST neovascularization angiostatic steroid delivery
IT Steroids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Angiostatic steroids methods and compds. for prevention and treatment of neovascularization)
IT Blood vessel, disease
(Osler-Wever syndrome; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)
IT Blood vessel, neoplasm
(angiofibroma; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)
IT Anti-inflammatory agents
Arteriosclerosis
Arthritis
Burn

Eye
Granulation
Neoplasm
Psoriasis
(angiostatic steroids methods and compns. for prevention and treatment of **neovascularization**)

IT Blood vessel, disease
(arteriovenous malformation; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT **Eye**
(cornea, graft; angiostatic steroids methods and compns. for prevention and treatment of **neovascularization**)

IT **Eye**
(cornea; angiostatic steroids methods and compns. for prevention and treatment of **neovascularization**)

IT Wound healing
(delayed; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT **Eye, disease**
(**diabetic retinopathy**; angiostatic steroids methods and compns. for prevention and treatment of **neovascularization**)

IT Joint, anatomical
(disease, hemophilic; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT Bone, disease
(fracture, nonunion; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT Blood vessel, neoplasm
(hemangioma; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT Shock (circulatory collapse)
(hemorrhagic; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT Skin, disease
(hypertrophic scar; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT Drug delivery systems
(injections, ophthalmic; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT **Glaucoma (disease)**
(neovascular; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT Angiogenesis
(neovascularization; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT Granuloma
(pyogenic; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT **Eye, disease**
(**retrolental fibroplasia**; angiostatic steroids methods and compns. for prevention and treatment of **neovascularization**)

IT Connective tissue
(scleroderma; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT Shock (circulatory collapse)
(septic; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT Neoplasm
(solid and pterigium; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT Drug delivery systems

(solns., ophthalmic; angiostatic steroids methods and compns. for prevention and treatment of neovascularization`)

IT Brain, disease
(stroke; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT Drug delivery systems
(suspensions, ophthalmic; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT Drug delivery systems
(topical; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT **Eye, disease**
(**trachoma**; angiostatic steroids methods and compns. for prevention and treatment of **neovascularization**)

IT Head
Spinal cord
(trauma; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT Shock (circulatory collapse)
(traumatic; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT Adhesion, physical
(vascular; angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT 149916-70-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT 149916-61-0P 149916-69-8P 160964-90-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT 53-02-1 57-63-6 68-23-5 68-60-0, Tetrahydrocortexolone 68-96-2, 17α-Hydroxyprogesterone 302-91-0 302-97-6 566-35-8, 11-Epicortisol 641-84-9 651-43-4 **7753-60-8** **10184-70-0** 15734-50-6 149916-56-3 149916-57-4 149916-59-6 149916-60-9 149916-62-1 149916-64-3 149916-65-4 149916-67-6 149952-80-7 149952-81-8 150213-68-6 160964-92-1, 21-Nor-5β-pregn-17(20)en-3α,16-diol 252684-24-5 252684-25-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT 58479-61-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

IT 149916-71-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD

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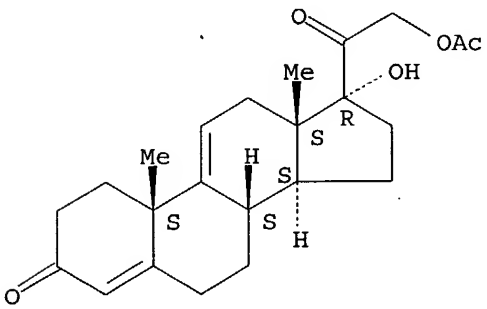
IT **7753-60-8 10184-70-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(angiostatic steroids methods and compns. for prevention and treatment of neovascularization)

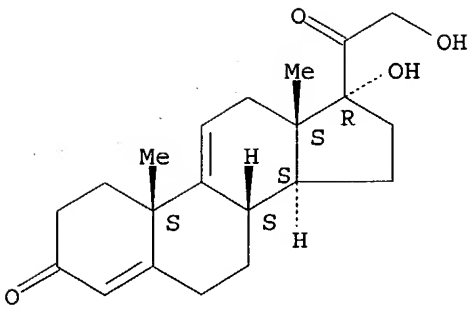
RN 7753-60-8 HCAPLUS
CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 10184-70-0 HCAPLUS
CN Pregna-4,9(11)-diene-3,20-dione, 17,21-dihydroxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 4 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:748307 HCAPLUS
DN 131:351535
ED Entered STN: 25 Nov 1999
TI synthesis and compositions of angiostatic agents for controlling ocular hypertension
IN Clark, Abbot F.
PA **Alcon Laboratories, Inc., USA**
SO U.S., 10 pp., Cont.-in-part of U.S. Ser. No. 990,424, abandoned.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-58
ICS A61K031-56
NCL 514172000
CC 32-5 (Steroids)
Section cross-reference(s): 1, 63
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5990099	A	19991123	US 1997-994114	19971219 <--
	US 4876250	A	19891024	US 1988-264918	19881031 <--
	US 5371078	A	19941206	US 1992-941485	19920908 <--
	US 5698545	A	19971216	US 1996-643387	19960506 <--
	WO 9903503	A1	19990128	WO 1998-US12711	19980618 <--
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	AU 734436	B2	20010614		
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	EP 1039912	B1	20020807		
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PRAI US 1988-264918	A1	19881031	<--		
US 1989-419226	B2	19891010	<--		
US 1990-559123	B2	19900727	<--		
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US 1994-349342	B1	19941202	<--		
US 1996-643387	A1	19960506	<--		
US 1997-990424	B2	19971215	<--		
US 1997-895184	A	19970716	<--		
US 1997-994114	A	19971219	<--		
WO 1998-US12711	W	19980618	<--		
WO 1998-US25913	W	19981207	<--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 5990099	ICM	A61K031-58
	ICS	A61K031-56
	NCL	514172000
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US 5371078	ECLA	A61K031/56; C07J041/00B; C07J041/00B4; C07J051/00; A61K031/565; A61K031/565; A61K031/565T10; A61K031/57; A61K031/57L5; A61K031/58; A61K031/58; A61K031/665; C07J003/00; C07J005/00C1; C07J009/00; C07J011/00 <--
US 5698545	ECLA	A61K031/565; A61K031/565; A61K031/565T10; A61K031/58; A61K031/665; C07J003/00; C07J005/00C1; C07J009/00; C07J011/00; C07J041/00B; C07J041/00B4; C07J051/00; A61K031/57; A61K031/57L5; A61K031/58 <--
WO 9932127	ECLA	A61K031/00; A61K031/56; A61K031/565; A61K031/565; A61K031/565T10; A61K031/57; A61K031/57L; A61K031/57L5; A61K031/58; A61K031/58; A61K031/665; C07J003/00; C07J005/00C1; C07J009/00; C07J011/00; C07J041/00B; C07J041/00B4; C07J051/00 <--

OS MARPAT 131:351535

AB Compns. of angiostatic agents for treating GLC1A glaucoma and methods for their use are disclosed. Preparation of selected steroid agents of the invention, e.g. 3β-acetamido-5β-pregnan-11β,17α,21-triol-20-one 21-acetate, is described.

ST GLC1A glaucoma steroid angiostatic agent prepn

IT Angiogenesis inhibitors
Antiglaucoma agents
(synthesis and compns. of angiostatic agents for controlling ocular hypertension)

IT 149916-69-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(synthesis and compns. of angiostatic agents for controlling ocular hypertension)

IT **7753-60-8P 10184-70-0P** 149916-61-0P 149916-70-1P
199583-00-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and compns. of angiostatic agents for controlling ocular hypertension)

IT 53-02-1, Tetrahydrocortisol
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and compns. of angiostatic agents for controlling ocular hypertension)
IT 149916-71-2P 150213-49-3P 150213-50-6P 160896-36-6P 160964-93-2P 250661-72-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and compns. of angiostatic agents for controlling ocular hypertension)
RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
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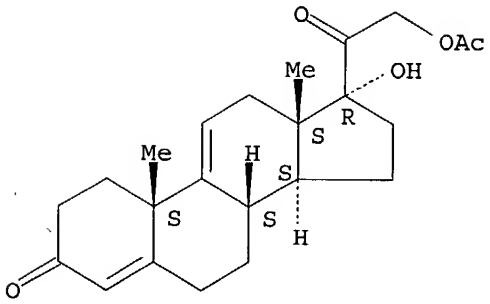
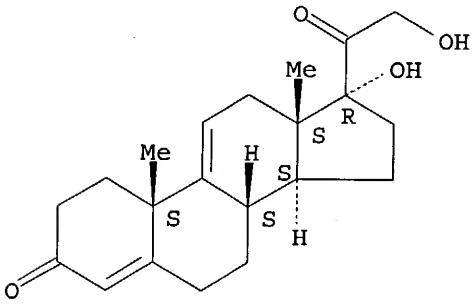
IT **7753-60-8P 10184-70-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and compns. of angiostatic agents for controlling ocular hypertension)
RN 7753-60-8 HCAPLUS
CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 10184-70-0 HCAPLUS
CN Pregna-4,9(11)-diene-3,20-dione, 17,21-dihydroxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 5 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:672339 HCAPLUS
DN 132:520
ED Entered STN: 22 Oct 1999
TI Angiostatic activity of steroids in the chick embryo CAM and rabbit cornea models of neovascularization
AU McNatt, Loretta G.; Weimer, Lori; Yanni, John; Clark, Abbot F.
CS **Alcon Laboratories, Inc., Fort Worth, TX, USA**
SO Journal of Ocular Pharmacology and Therapeutics (**1999**), 15(5), 413-423
CODEN: JOPTFU; ISSN: 1080-7683
PB Mary Ann Liebert, Inc.
DT Journal
LA English
CC 2-2 (Mammalian Hormones)
Section cross-reference(s): 12
AB Ocular neovascular diseases represent a major cause of blindness in the world. Angiostatic steroids are a unique class of compds. which inhibit the formation of new blood vessels in various models, including ocular models of angiogenesis. In search of potent new anti-angiogenic agents for the treatment of ocular neovascular disease, a large group of steroids were evaluated for angiostatic activity in the chick embryo CAM model. Angiostatic activity was found among all steroid classes included in the study. There was a good correlation between the angiostatic efficacies of 15 diverse steroids tested in the chick CAM and in the rabbit LPS-induced corneal pocket models of neovascularization ($r=0.76$, $p=0.01$). These studies show that potent angiostatic steroids inhibit neovascularization in two different animal models, suggesting a common mechanism of action. Glucocorticoid therapy is sometimes associated with ocular side effects. Two

of the most potent angiostatic steroids, **AL-3789** and **AL-4940**, were evaluated for glucocorticoid-mediated anti-inflammatory activity in the in vitro U937 cell model of LPS-induced IL-1 induction and found to be devoid of glucocorticoid activity. Angiostatic steroids which lack glucocorticoid activity should be attractive drug candidates for treating ocular neovascular disease.

ST steroid **AL3789** angiostatic structure activity neovascularization; **AL4940** steroid angiostatic structure activity neovascularization; glucocorticoid antiinflammatory steroid angiostatic neovascularization; chicken rabbit neovascularization model steroid angiostatic

IT Angiogenesis inhibitors
Anti-inflammatory agents
Chicken (Gallus domesticus)
Embryo, animal
(angiostatic activity of steroids in chick embryo CAM and rabbit cornea models of neovascularization)

IT Glucocorticoids
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(angiostatic activity of steroids in chick embryo CAM and rabbit cornea models of neovascularization)

IT Structure-activity relationship
(angiostatic; angiostatic activity of steroids in chick embryo CAM and rabbit cornea models of neovascularization)

IT **Eye**
(cornea; angiostatic activity of steroids in chick embryo CAM and rabbit cornea models of **neovascularization**)

IT Angiogenesis
Angiogenesis
(neovascularization, eye; angiostatic activity of steroids in chick embryo CAM and rabbit cornea models of neovascularization)

IT **Eye, disease**
(**neovascularization**; angiostatic activity of steroids in chick embryo CAM and rabbit cornea models of **neovascularization**)

IT **7753-60-8, AL-3789 10184-70-0, AL 4940**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(angiostatic activity of steroids in chick embryo CAM and rabbit cornea models of neovascularization)

IT 50-02-2, Dexamethasone 50-23-7, Cortisol 50-24-8, Prednisolone
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(angiostatic activity of steroids in chick embryo CAM and rabbit cornea models of neovascularization)

IT 50-28-2, 17β-Estradiol, biological studies 53-02-1 57-63-6, 17α-Ethynylestradiol 58-18-4, 17α-Methyltestosterone 58-22-0, Testosterone 68-22-4, Norethindrone 68-23-5, Norethynodrel 68-42-8 68-60-0 72-33-3, Mestranol 302-91-0, AL 3308 302-97-6, AL 3793 362-07-2, 2-Methoxyestradiol 434-03-7, Ethisterone 520-85-4, Medroxyprogesterone 641-84-9, AL 3841 1516-47-8, AL 3685 88729-26-4, AL 3855 105384-40-5, U-42129 111320-97-9, U 73843 149916-54-1, AL 3913 149916-56-3, AL 3914 149916-59-6, AL 4989 149916-62-1, AL 4988 149916-69-8, AL 4063 149916-70-1, AL 3806 251297-08-2, AL 4710 251297-11-7, U 87096 251297-13-9, AL 4772 251297-16-2, AL 5267
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(angiostatic activity of steroids in chick embryo CAM and rabbit cornea models of neovascularization)

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD

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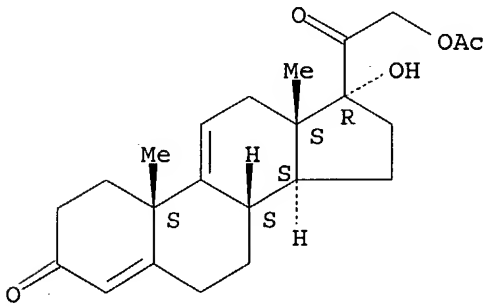
IT **7753-60-8, AL-3789 10184-70-0, AL 4940**

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(angiostatic activity of steroids in chick embryo CAM and rabbit cornea models of neovascularization)

RN 7753-60-8 HCAPLUS

CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

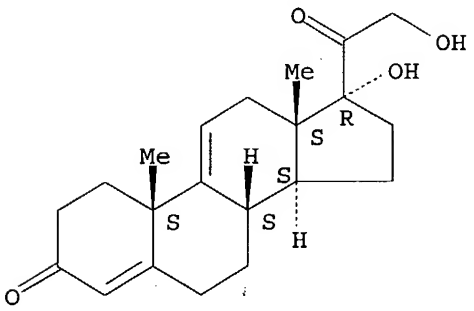


RN 10184-70-0 HCAPLUS

CN Pregna-4,9(11)-diene-3,20-dione, 17,21-dihydroxy- (7CI, 8CI, 9CI) (CA

INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 6 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:425760 HCAPLUS
DN 131:54038
ED Entered STN: 09 Jul 1999
TI Steroidal angiostatic agents and compositions for controlling GLC1A glaucoma, compositions, and preparation thereof
IN Clark, Abbot F.
PA **Alcon Laboratories, Inc., USA**
SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-57
ICS A61K031-575; A61K031-56
CC 1-12 (Pharmacology)
Section cross-reference(s): 2, 32, 63
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9932127	A1	19990701	WO 1998-US25913	19981207 <--
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	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
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	WO 9903503	A1	19990128	WO 1998-US12711	19980618 <--
	W: AU, BR, CA, JP, MX, US				
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	AU 734195	B2	20010607		
	EP 1003553	A1	20000531	EP 1998-931367	19980618 <--
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	JP 2001510170	T2	20010731	JP 2000-502798	19980618 <--
	CA 2315829	AA	19990701	CA 1998-2315829	19981207 <--
	AU 9917142	A1	19990712	AU 1999-17142	19981207 <--
	AU 734436	B2	20010614		
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	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
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	AT 221781	E	20020815	AT 1998-961956	19981207 <--

	MX 9911140	A	20000430	MX 1999-11140	19991202	<--
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	US 1989-419226	B2	19891010	<--		
	US 1990-559123	B2	19900727	<--		
	US 1992-941485	A1	19920908	<--		
	US 1994-349342	B1	19941202	<--		
	US 1996-643387	A1	19960506	<--		
	US 1997-895184	A	19970716	<--		
	US 1997-990424	B2	19971215	<--		
	WO 1998-US12711	W	19980618	<--		
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CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9932127	ICM	A61K031-57
	ICS	A61K031-575; A61K031-56
WO 9932127	ECLA	A61K031/00; A61K031/56; A61K031/565; A61K031/565; A61K031/565T10; A61K031/57; A61K031/57L; A61K031/57L5; A61K031/58; A61K031/58; A61K031/665; C07J003/00; C07J005/00C1; C07J009/00; C07J011/00; C07J041/00B; C07J041/00B4; C07J051/00 <--
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OS MARPAT 131:54038

AB Compns. of steroid angiostatic agents for treating GLC1A glaucoma and methods for their use are disclosed. Preparation of selected steroid agents of the invention , e.g. 3β-acetamido-21-acetoxy-5β-pregnan-11β,17α-diol-20-one, is described.

ST GLC1A glaucoma steroid angiostatic agent prepn

IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GLC1A; steroidal angiostatic agents and compns. for controlling GLC1A glaucoma, compns., and preparation)

IT Angiogenesis inhibitors
Antiglaucoma agents
Drug delivery systems
(steroidal angiostatic agents and compns. for controlling GLC1A glaucoma, compns., and preparation)

IT 149916-71-2P 150213-50-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction; steroidal angiostatic agents and compns. for controlling GLC1A glaucoma, compns., and preparation)

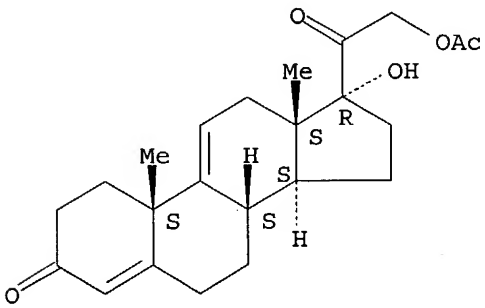
IT 53-02-1 6160-65-2, Thiocarbonyl diimidazole 58479-61-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; steroidal angiostatic agents and compns. for controlling GLC1A glaucoma, compns., and preparation)

IT 149916-69-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(steroidal angiostatic agents and compns. for controlling GLC1A glaucoma, compns., and preparation)

IT 149916-61-0P 149916-70-1P 199583-00-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(steroidal angiostatic agents and compns. for controlling GLC1A

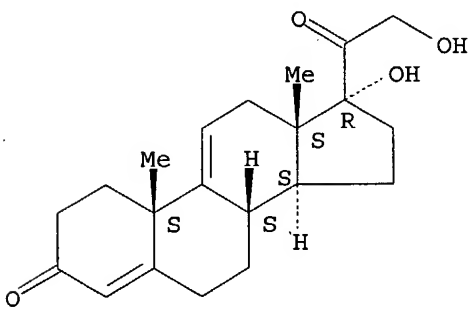
glaucoma, compns., and preparation)
IT **7753-60-8 10184-70-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(steroidal angiostatic agents and compns. for controlling GLC1A glaucoma, compns., and preparation)
IT 228397-21-5P
RL: BYP (Byproduct); PREP (Preparation)
(steroidal angiostatic agents and compns. for controlling GLC1A glaucoma, compns., and preparation)
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Alcon Lab Inc; WO 9310141 A 1993 HCAPLUS
(2) Clark Abbot, F; US 4876250 A 1989 HCAPLUS
(3) Clark Abbot, F; US 5371078 A 1994 HCAPLUS
(4) Clark Abbot, F; US 5698545 A 1997 HCAPLUS
(5) Univ Duke; WO 9518621 A 1995 HCAPLUS
(6) Upjohn Co; WO 9119731 A 1991 HCAPLUS
IT **7753-60-8 10184-70-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(steroidal angiostatic agents and compns. for controlling GLC1A glaucoma, compns., and preparation)
RN 7753-60-8 HCAPLUS
CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 10184-70-0 HCAPLUS
CN Pregna-4,9(11)-diene-3,20-dione, 17,21-dihydroxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:795450 HCAPLUS
DN 128:136567
ED Entered STN: 20 Dec 1997
TI **AL-3789**: a novel ophthalmic angiostatic steroid
AU Clark, Abbot F.
CS **Alcon Lab., Fort worth, TX, 76134, USA**
SO Expert Opinion on Investigational Drugs (**1997**), 6(12), 1867-1877
CODEN: EOIDER; ISSN: 0967-8298
PB Ashley Publications
DT Journal; General Review
LA English
CC 2-0 (Mammalian Hormones)
Section cross-reference(s): 1
AB A review with 27 refs. Ocular neovascular diseases are a leading cause of blindness in the world. Research is beginning to unravel the complex mechanisms involved in the pathogenesis of ocular neovascular diseases, but currently there are very few methods for the effective treatment of these blinding disorders. **AL-3789** (Alcon Labs.) is an angiostatic steroid which shows significant activity in inhibiting new blood vessel formation in a wide variety of models of neovascularization, including neovascularization in ocular tissues. This angiostatic steroid has broad angiostatic activity and is effective in a number of different animal species and tissues, regardless of the angiogenic stimulus. **AL-3789** is devoid of conventional steroid hormone activity and does not appear to have any other pharmacol. side-effects at the doses and routes of administration tested. In preclin. safety studies, **AL-3789** has no apparent ocular or systemic toxicity when dosed chronically by topical ocular or by systemic administration. It remains to be seen whether these promising results will be confirmed in clin. studies.
ST review angiostatic **AL 3789** ocular neovascularization
IT Angiogenesis inhibitors
Eye
(**AL-3789** as a novel ophthalmic angiostatic steroid for treatment of ocular disorders resulting from **neovascularization**)
IT Angiogenesis
(neovascularization; **AL-3789** as a novel ophthalmic angiostatic steroid for treatment of ocular disorders resulting from neovascularization)
IT **7753-60-8, AL 3789**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**AL-3789** as a novel ophthalmic angiostatic steroid for treatment of ocular disorders resulting from neovascularization)
RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Adamis, A; Arch Ophthalmol 1996, V114, P66 HCAPLUS
(2) Aiello, L; Arch Ophthalmol 1996, V114(10), P1252 MEDLINE
(3) Aiello, L; Proc Natl Acad Sci USA 1995, V92(23), P10457 HCAPLUS
(4) Ashino-Fuse, H; Int J Cancer 1989, V44, P859 HCAPLUS
(5) Avery, R; Arch Ophthalmol 1990, V108, P1474 MEDLINE
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(7) Blei, F; J Cell Physiol 1993, V155, P568 HCAPLUS
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(10) Crum, R; Science 1985, V230, P1375 HCAPLUS
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(12) D'Amato, R; Proc Natl Acad Sci USA 1994, V91, P4082 HCAPLUS
(13) Folkman, J; New Engl J Med 1995, V333, P1757 MEDLINE

(14) Friedlander, M; Proc Natl Acad Sci USA 1996, V93, P9764 HCAPLUS
(15) Friedlander, M; Science 1995, V270, P1500 HCAPLUS
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(17) Guyer, D; Arch Ophthalmol 1997, V115, P865
(18) Kusaka, M; Biochem Biophys Res Comm 1991, V174, P1070 HCAPLUS
(19) LI, W; Invest Ophthalmol Vis Sci 1991, V32, P2898 MEDLINE
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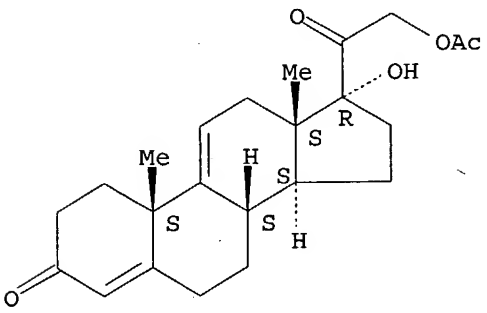
(21) McNatt, L; J Steroid Biochem Mol Biol 1992, V42(7), P687 HCAPLUS
(22) Miller, J; Ophthalmology 1993, V100, P9 MEDLINE
(23) Proia, A; Exp Eye Res 1993, V57, P693 HCAPLUS
(24) Robinson, G; Proc Natl Acad Sci USA 1996, V93, P4851 HCAPLUS
(25) Shima, D; Mol Med 1995, V1(2), P182 HCAPLUS
(26) Smith, L; Science 1997, V276, P1706 HCAPLUS
(27) Tolman, B; Invest Ophthalmol Vis Sci 1995, V36(4), P454

IT **7753-60-8, AL 3789**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**AL-3789** as a novel ophthalmic angiostatic steroid for treatment of ocular disorders resulting from neovascularization)
RN 7753-60-8 HCAPLUS
CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:745948 HCAPLUS
DN 128:39554
ED Entered STN: 27 Nov 1997
TI Use of steroid compounds to prevent non-cancerous tissue growth
IN Clark, Abbot F.; Goode, Stephen M.
PA **Alcon Laboratories, Inc., USA**
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-565
ICS A61K031-57
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 2
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9741867	A1	19971113	WO 1997-US2809	19970221 <--
	W: AU, CA, JP, MX				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9719701	A1	19971126	AU 1997-19701	19970221 <--
PRAI	US 1996-19060P	P	19960509 <--		

WO 1997-US2809 W 19970221 <--

CLASS PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9741867	ICM	A61K031-565
	ICS	A61K031-57

OS MARPAT 128:39554

AB Disclosed are pregnane analogs for use in preventing non-cancerous tissue growth and pharmaceutical compns. containing them. For example, an ocular solution contained 21-nor-5β-pregnan-3α,17α,20-triol-3-phosphate 1, benzalkonium chlorides 0.01, HPMC 0.5, NaCl 0.8, Na phosphate 0.28, di-Na edetate 0.01 %, NaOH/HCl q.s. to pH 7.2, and purified water to 100 %.

ST pregnane steroid noncancerous tissue growth prevention

IT **Glaucoma (disease)**
(filtration bleb failure; steroids for prevention of noncancerous tissue growth)

IT Keratosis
(hyperkeratosis; steroids for prevention of noncancerous tissue growth)

IT Drug delivery systems
(ointments, creams; steroids for prevention of noncancerous tissue growth)

IT Drug delivery systems
(ointments; steroids for prevention of noncancerous tissue growth)

IT Neoplasm
(polyps; steroids for prevention of noncancerous tissue growth)

IT **Eye, disease**
(pterygium; steroids for prevention of noncancerous tissue growth)

IT Drug delivery systems
(solns., ophthalmic; steroids for prevention of noncancerous tissue growth)

IT Keloid
Wound healing
(steroids for prevention of noncancerous tissue growth)

IT Progestogens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(steroids for prevention of noncancerous tissue growth)

IT Drug delivery systems
(suppositories; steroids for prevention of noncancerous tissue growth)

IT Drug delivery systems
Drug delivery systems
(suspensions, ophthalmic; steroids for prevention of noncancerous tissue growth)

IT Drug delivery systems
(tablets; steroids for prevention of noncancerous tissue growth)

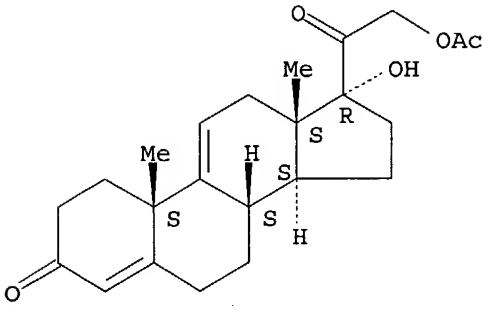
IT 57-63-6 68-23-5 302-97-6 **7753-60-8 10184-70-0**
149916-54-1 149916-55-2 149916-56-3 149916-57-4 149916-58-5
149916-59-6 149916-60-9 149916-62-1 149916-69-8 199583-00-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(steroids for prevention of noncancerous tissue growth)

IT **7753-60-8 10184-70-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(steroids for prevention of noncancerous tissue growth)

RN 7753-60-8 HCAPLUS

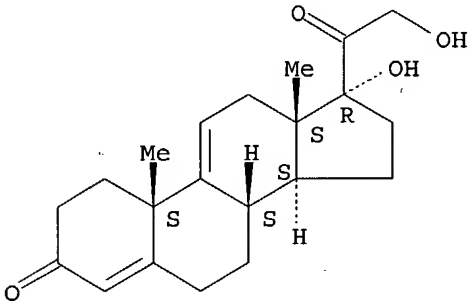
CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 10184-70-0 HCAPLUS
CN Pregna-4,9(11)-diene-3,20-dione, 17,21-dihydroxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 9 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:704225 HCAPLUS
DN 128:57124
ED Entered STN: 08 Nov 1997
TI Mechanism of action and clinical efficacy of **AL-3789**, an angiostatic steroid (neovascularization, pterygium, tumor growth)
AU Defaller, Joseph Michael
CS Health Science Center, Univ. of North Texas, Fort Worth, TX, USA
SO **(1996)** 115 pp. Avail.: UMI, Order No. DA9735970
From: Diss. Abstr. Int., B 1997, 58(6), 2974
DT Dissertation
LA English
CC 1-6 (Pharmacology)
AB Unavailable
ST **AL3789** steroid angiostasis neovascularization tumor pterygium
IT Angiogenesis inhibitors
Antitumor agents
(angiostatic steroid **AL-3789** mechanism and clin. efficacy)
IT Angiogenesis
(neovascularization; angiostatic steroid **AL-3789** mechanism and clin. efficacy)
IT **Eye, disease**
(pterygium; angiostatic steroid **AL-3789** mechanism and clin. efficacy)
IT **7753-60-8, AL 3789**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

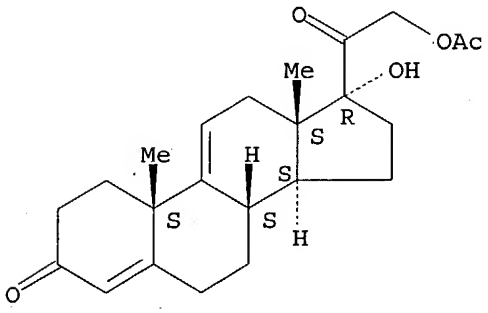
(Uses)
(angiostatic steroid **AL-3789** mechanism and clin. efficacy)

IT **7753-60-8, AL 3789**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(angiostatic steroid **AL-3789** mechanism and clin. efficacy)

RN 7753-60-8 HCAPLUS

CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 10 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:294615 HCAPLUS

DN 122:114929

ED Entered STN: 14 Jan 1995

TI Angiostatic steroids and methods and compositions for controlling ocular hypertension

IN Clark, Abbot F.; Conrow, Raymond E.

PA **Alcon Laboratories, Inc., USA**

SO U.S., 10 pp. Cont.-in-part of U.S. Ser. No. 559, 123, abandoned.
CODEN: USXXAM

DT Patent

LA English

IC ICM A61K031-56

NCL 514182000

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 32

FAN.CNT 7

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5371078	A	19941206	US 1992-941485	19920908 <--
US 4876250	A	19891024	US 1988-264918	19881031 <--
WO 9310141	A2	19930527	WO 1992-US10133	19921123 <--
WO 9310141	A3	19930902		
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RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
AU 9332235	A1	19930615	AU 1993-32235	19921123 <--
AU 678961	B2	19970619		
EP 614463	A1	19940914	EP 1993-900609	19921123 <--
EP 614463	B1	20030212		
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JP 07501081	T2	19950202	JP 1993-509563	19921123 <--
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     US 5990099          A     19991123    US 1997-994114        19971219 <--
     WO 9903503          A1    19990128    WO 1998-US12711       19980618 <--
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        RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
            PT, SE
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     AU 734195           B2    20010607
     EP 1003553          A1    20000531    EP 1998-931367        19980618 <--
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            IE, FI
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     HK 1012638          A1    20030509    HK 1998-113831        19981217 <--
     MX 9911140          A     20000430    MX 1999-11140         19991202 <--
PRAI US 1988-264918      A1    19881031  <--
     US 1989-419226      B2    19891010  <--
     US 1990-559123      B2    19900727  <--
     US 1991-796169      A     19911122  <--
     US 1992-892448      A     19920602  <--
     US 1992-941485      A     19920908  <--
     EP 1993-900609      A3    19921123  <--
     WO 1992-US10133     A     19921123  <--
     US 1994-349342      B1    19941202  <--
     US 1996-643387      A1    19960506  <--
     US 1997-895184      A     19970716  <--
     US 1997-990424      B2    19971215  <--
     WO 1998-US12711     W     19980618  <--
CLASS
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                 NCL    514182000
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                        A61K031/565; A61K031/565; A61K031/565T10; A61K031/57;
                        A61K031/57L5; A61K031/58; A61K031/58; A61K031/665;
                        C07J003/00; C07J005/00C1; C07J009/00; C07J011/00    <--
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                        A61K031/57L5; A61K031/58; A61K031/58; A61K031/665;
                        C07J003/00; C07J005/00C1; C07J009/00; C07J011/00;
                        C07J041/00B; C07J041/00B4; C07J051/00; A61K031/565  <--
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                        A61K031/665; C07J003/00; C07J005/00C1; C07J009/00;
                        C07J011/00; C07J041/00B; C07J041/00B4; C07J051/00;
                        A61K031/57; A61K031/57L5; A61K031/58                <--
 US 5990099      ECLA   A61K031/56; A61K031/565; A61K031/565; A61K031/565T10;
                        A61K031/57; A61K031/57L5; A61K031/58; A61K031/58;
                        A61K031/665; C07J003/00; C07J005/00C1; C07J009/00;
                        C07J011/00; C07J041/00B; C07J041/00B4; C07J051/00   <--
OS   MARPAT 122:114929
AB   Pharmaceutical compns. of the angiostatic steroids and methods for their
     use in treating ocular hypertension, including controlling the ocular
     hypertension associated with primary open-angle glaucoma, are disclosed.  In
     addition, the combination of the compds. with glucocorticoids for the
     prevention of elevated IOP during the treatment of inflammation is
     disclosed.  For example, 21-methyl-5β-pregnan-
     3α,11β,17α,21-tetrol-20-one 21-Me ether (I) was prepared
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from tetrahydrocortisol F. An ophthalmic composition contained I 1.0, tyloxapol 0.01-0.05, HPMC 0.5, benzalkonium chloride 0.01, NaCl 0.8, di-Na edetate 0.01%, NaOH/HCl q.s. to pH 7.4, and purified water to 100 mL.

ST ophthalmic angiostatic steroid glaucoma; ocular hypertension angiogenesis inhibitor steroid

IT Steroids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(angiostatic steroids for controlling ocular hypertension)

IT Inflammation inhibitors
(glucocorticoids; angiostatic steroids for prevention of elevated intraocular pressure during treatment of inflammation)

IT Corticosteroids, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(gluco-, angiostatic steroids for prevention of elevated intraocular pressure during treatment of inflammation)

IT Pharmaceutical dosage forms
(ophthalmic, angiostatic steroids for controlling ocular hypertension)

IT **Glaucoma (disease)**
(primary open-angle, angiostatic steroids for controlling ocular hypertension)

IT 160964-90-9P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(angiostatic steroids for controlling ocular hypertension)

IT 57-63-6 68-23-5 302-97-6 641-84-9 **7753-60-8** 149916-54-1
149916-56-3 149916-57-4 149916-59-6 149916-60-9 149916-61-0
149916-62-1 149916-64-3 149916-65-4 149916-66-5 149916-67-6
149916-69-8 149952-80-7 149952-81-8 150213-68-6 160896-34-4
160964-91-0 160964-92-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(angiostatic steroids for controlling ocular hypertension)

IT 50-02-2, Dexamethasone
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(angiostatic steroids for prevention of elevated intraocular pressure during treatment of inflammation)

IT 53-02-1, Tetrahydrocortisol 58479-61-1, tert-Butyldiphenylchlorosilane 149916-69-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of angiostatic steroids for controlling ocular hypertension)

IT 149916-71-2P 150213-49-3P 150213-50-6P 160896-36-6P 160964-93-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of angiostatic steroids for controlling ocular hypertension)

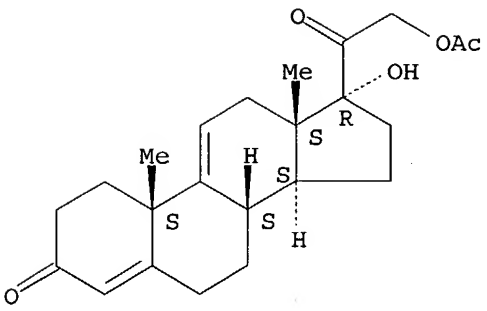
IT 149916-70-1P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of angiostatic steroids for controlling ocular hypertension)

IT **7753-60-8**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(angiostatic steroids for controlling ocular hypertension)

RN 7753-60-8 HCAPLUS

CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:560646 HCAPLUS
DN 119:160646
ED Entered STN: 16 Oct 1993
TI Preparation and formulation of angiostatic steroids
IN Clark, Abbot F.; Conrow, Raymond E.
PA **Alcon Laboratories, Inc., USA**
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07J005-00
ICS A61K031-56; C07J003-00; C07J051-00; C07J011-00; C07J009-00; C07J041-00
CC 32-5 (Steroids)
Section cross-reference(s): 1, 63
FAN.CNT 7

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	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE					
	US 5371078	A	19941206	US 1992-941485	19920908	<--
	AU 9332235	A1	19930615	AU 1993-32235	19921123	<--
	AU 678961	B2	19970619			
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	EP 614463	B1	20030212			
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	JP 3378245	B2	20030217			
	AT 232540	E	20030215	AT 1993-900609	19921123	<--
	US 5679666	A	19971021	US 1994-342524	19941121	<--
	US 5770592	A	19980623	US 1997-895184	19970716	<--
	WO 9903503	A1	19990128	WO 1998-US12711	19980618	<--
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	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
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	AU 734195	B2	20010607			
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	JP 2001510170	T2	20010731	JP 2000-502798	19980618	<--
	HK 1012638	A1	20030509	HK 1998-113831	19981217	<--
	MX 9911140	A	20000430	MX 1999-11140	19991202	<--
	US 6297228	B1	20011002	US 1999-445237	19991202	<--

PRAI US 1991-796169 A 19911122 <--
US 1992-892448 A 19920602 <--
US 1992-941485 A 19920908 <--
US 1988-264918 A1 19881031 <--
US 1989-419226 B2 19891010 <--
US 1990-559123 B2 19900727 <--
WO 1992-US10133 A 19921123 <--
US 1994-342524 A1 19941121 <--
US 1997-895184 A 19970716 <--
WO 1998-US12711 W 19980618 <--

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9310141	ICM	C07J005-00
	ICS	A61K031-56; C07J003-00; C07J051-00; C07J011-00; C07J009-00; C07J041-00
US 5371078	ECLA	A61K031/56; C07J041/00B; C07J041/00B4; C07J051/00; A61K031/565; A61K031/565; A61K031/565T10; A61K031/57; A61K031/57L5; A61K031/58; A61K031/58; A61K031/665; C07J003/00; C07J005/00C1; C07J009/00; C07J011/00 <--

OS MARPAT 119:160646

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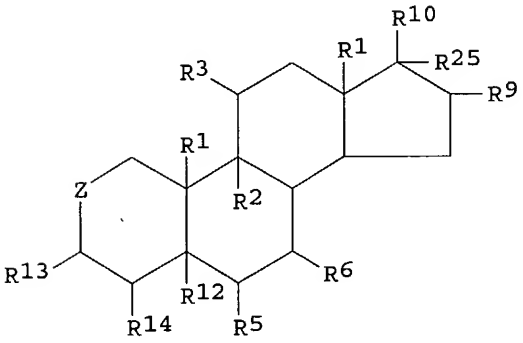

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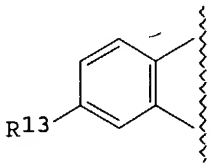


II

AB Title compds. [I and II; R1 = H, β-Me, β-Et, R2 = H, F, Cl; R3 = H, alkoxy, alkanoyloxy, halo, O2CNH2, etc.; R2R3 = bond, O; R5 = H, OH, halo, Me, Ph, vinyl, alkyl, R6 = H, Me; R9 = H, OH, Me, F, 2-(alkoxy)ethyl, 2-(alkanoyloxy)ethyl, etc.; R10 = H, C.tplbond.CH, vinyl, halo, OH, Me, etc.; R12 = H; R1R12 = bond; R13 = H, OH, alkoxy, NH2, etc.; R14 = H; R12R14 = bond; R25 = OH, alkoxy, alkanoyloxy, CO2H, CH2OH, etc.; Z = CHR4, etc.; R4 = H, Me, Cl, F] were prepared Thus, tetrahydrocortisol-F was converted in 3 steps to 5β-pregnan-11β,17α,21-triol-2-one. 4,9(11)-Pregnadiene-17α,21-diol-3,20-dione gave complete inhibition of lipopolysaccharide-induced corneal neovascularization in rabbit eye at 50 μg in a pellet implant.

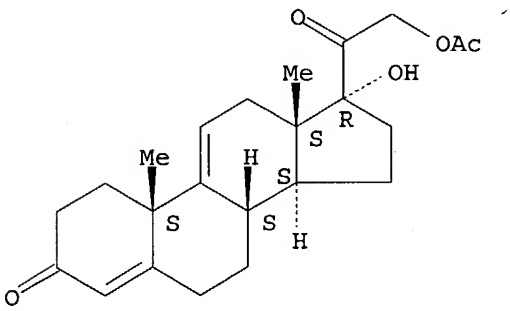
ST steroid prepn angiostatic; ocular hypertension treatment angiostatic steroid

IT **Eye**
(disease, neovascularization, treatment of, angiostatic steroids for)

IT Arteriosclerosis
Arthritis
Burn
Glaucoma (disease)
Granulation
Neoplasm

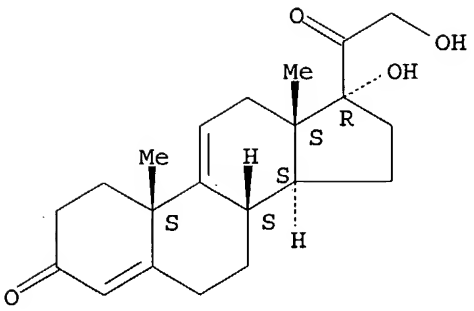
Shock
Wound healing
(prevention of neovascularization in, angiostatic steroids for)
IT Blood vessel, neoplasm
(angiofibroma, prevention of neovascularization in, angiostatic steroids for)
IT Blood vessel, neoplasm
(hemangioma, treatment of, angiostatic steroids for)
IT Blood vessel, disease
(neovascularization, treatment of, angiostatic steroids for)
IT Injury
(trauma, prevention of neovascularization in, angiostatic steroids for)
IT 57-63-6 68-23-5 68-60-0 302-97-6 566-35-8 633-29-4
7753-60-8 10184-70-0
RL: PROC (Process)
(formulation of, as angiostatic agent)
IT 149916-71-2P 150213-49-3P 150213-50-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and reaction. of, in preparation of angiostatic agent)
IT 641-84-9P 149916-54-1P 149916-55-2P 149916-56-3P 149916-57-4P
149916-58-5P 149916-59-6P 149916-60-9P 149916-61-0P 149916-62-1P
149916-63-2P 149916-64-3P 149916-65-4P 149916-66-5P 149916-67-6P
149916-68-7P 149916-69-8P 149916-70-1P 149952-80-7P 149952-81-8P
150213-68-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as angiostatic agent)
IT 53-02-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction. of, in preparation of angiostatic agent)
IT **7753-60-8 10184-70-0**
RL: PROC (Process)
(formulation of, as angiostatic agent)
RN 7753-60-8 HCAPLUS
CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 10184-70-0 HCAPLUS
CN Pregna-4,9(11)-diene-3,20-dione, 17,21-dihydroxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 12 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:152156 HCAPLUS
DN 116:152156
ED Entered STN: 17 Apr 1992
TI Preparation of 17a,21-dihydroxypregna-4,9(11)-diene-3,20-diones and analogs as angiogenesis inhibitors
IN Wilks, John William; Dekoning, Thomas Frank; Aristoff, Paul Adrian
PA Upjohn Co., USA
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07J031-00
ICS C07J009-00; C07J051-00; C07J007-00; C07J005-00; A61K031-56
ICA C07J003-00; C07J071-00
CC 32-5 (Steroids)
Section cross-reference(s): 1
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PI	WO 9119731	A1	19911226	WO 1991-US3459	19910523 <--
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	RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
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	CA 2081205	C	20010227		
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	AU 657690	B2	19950323		
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	JP 05507912	T2	19931111	JP 1991-509678	19910523 <--
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	HK 1013078	A1	20000929	HK 1998-114206	19981221 <--
	GR 3033524	T3	20000929	GR 2000-401215	20000526 <--
PRAI	US 1990-536894	A	19900611 <--		
	US 1990-609661	A2	19901106 <--		
	WO 1991-US3459	A	19910523 <--		
	US 1994-178172	B1	19940106 <--		
	US 1994-308061	B1	19940916 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
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	ICS	C07J009-00; C07J051-00; C07J007-00; C07J005-00; A61K031-56

ICA C07J003-00; C07J071-00
OS MARPAT 116:152156
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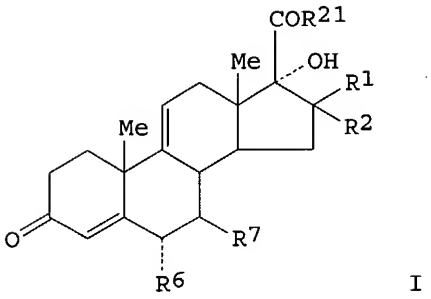
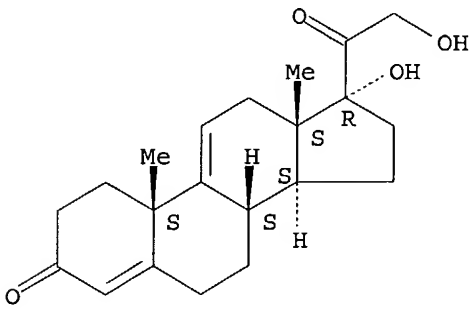


I

AB Title compds. [I; 1 of R1,R2 = H and the other = H or Me; R6 = H, F, Me; R7 = H, Me; R21 = CR213R214OR211, CR212R213SR211, CH2Br, etc.; R211 = H, P(O)(OH)2, COR212; R212 = alkyl; R213,R214 = H, alkyl] were prepared as angiogenesis inhibitors (no data). Thus, 17α,21-dihydroxypregna-4,9(11)-diene-3,20-dione 21-acetate was hydrolyzed to give 17α,21-dihydroxypregna-4,9(11)-diene-3,20-dione.
ST pregnadienedione dihydroxy prepn angiogenesis inhibitor; hydroxypregnadienedione prepn angiogenesis inhibitor
IT Antidiabetics and Hypoglycemics
Neoplasm inhibitors
Parasiticides
(angiogenesis-inhibiting dihydroxypregnadienediones)
IT Ovarian cycle
(disruption of, treatment of, angiogenesis-inhibiting dihydroxypregnadienediones for)
IT Blood vessel
(formation of, inhibition of, dihydroxypregnadienediones and analogs for)
IT Embryo
(implantation of, inhibition of, angiogenesis-inhibiting dihydroxypregnadienediones and analogs for)
IT Burn
Glaucoma (disease)
Psoriasis
(treatment of, angiogenesis-inhibiting dihydroxypregnadienediones for)
IT Inflammation inhibitors
(antiarthritics, angiogenesis-inhibiting dihydroxypregnadienediones)
IT Antiarteriosclerotics
(antiatherosclerotics, angiogenesis-inhibiting dihydroxypregnadienediones)
IT **Eye, disease**
(**neovascularization**, prevention of, angiogenesis-inhibiting dihydroxypregnadienediones for)
IT 133694-55-0P 133694-62-9P 133694-63-0P 133694-65-2P 139667-54-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of angiogenesis inhibitors)
IT 378-61-0P 10184-69-7P **10184-70-0P** 19788-80-8P 50630-13-2P
88903-68-8P 103924-17-0P 111245-54-6P 133694-58-3P 133694-67-4P
139667-52-0P 139667-53-1P 139667-55-3P 139692-60-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as angiogenesis inhibitor)
IT 1881-07-8 **7753-60-8** 105384-40-5
RL: RCT (Reactant); RACT (Reactant or reagent)

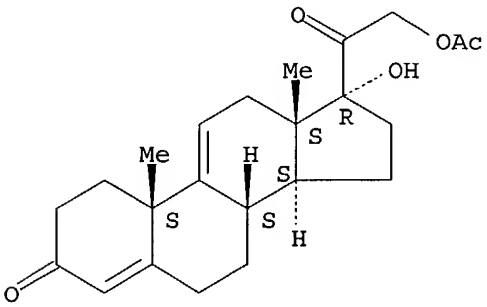
(reaction of, in preparation of angiogenesis inhibitors)
IT **10184-70-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as angiogenesis inhibitor)
RN 10184-70-0 HCAPLUS
CN Pregna-4,9(11)-diene-3,20-dione, 17,21-dihydroxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **7753-60-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of angiogenesis inhibitors)
RN 7753-60-8 HCAPLUS
CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 13 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:687178 HCAPLUS
DN 115:287178
ED Entered STN: 27 Dec 1991
TI Ophthalmic composition of angiostatic steroid-glucocorticoid combination for treatment of inflammation
IN Clark, Abbot F.
PA **Alcon Laboratories, Inc., USA**
SO PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-58
ICS A61K031-56
CC 63-6 (Pharmaceuticals)
FAN.CNT 7

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PI	WO 9103245	A1	19910321	WO 1990-US4071	19900725 <--
	W: AU, CA, JP				
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	AU 9062952	A1	19910408	AU 1990-62952	19900725 <--
	AU 637824	B2	19930610		
	EP 489779	A1	19920617	EP 1990-912700	19900725 <--
	EP 489779	B1	19980128		
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	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
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CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
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	ICS	A61K031-56

OS MARPAT 115:287178

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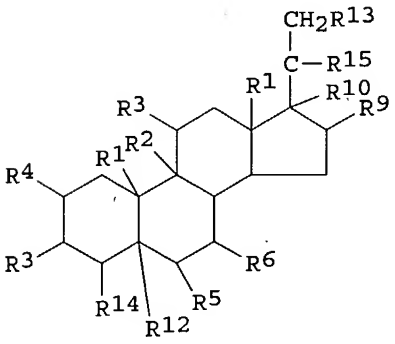


I

AB Pharmaceutical compns. useful in the treatment of ophthalmic inflammation, and methods of treating ophthalmic inflammation with those compns., are disclosed. The compns. contain a combination of a glucocorticoid and an angiostatic steroid, e.g. I [R1 = β-Me, β-Et; R2 = H, Cl; R3 = H, OH, alkoxy, etc., or R2R3 = O or double bond bridging C-9 and C-11, or R2 = α-F and R3 = β-OH, or R2 = α-Cl and R3 = β-Cl; R4 = H, Me, Cl, F; R5 = H, OH, F, Cl, Br, Me, Ph, vinyl, alkyl; R6 = H, Me; R9 = H, OH, Me, F, :CH2; R10 = H, OH, Me, or R10 forms a 2nd bond between C-16 and C-17; R12 = H or double bond with R14; R13 = H, OH, :O, OP(O)(OH)2, OC(O)(CH2)nCO2H (n = 2-6); R14 = H, double bond with R12; R15

= :O, OH; R23 = OH, OPO(O)(OH)2, etc. (with provisions and exclusions)]. The angiostatic steroid substantially prevents any significant increases in intraocular pressure which might otherwise be experienced by the patient as a side effect of the glucocorticoid component of the compns. The therapeutic interaction of the 2 components therefore allows the potent anti-inflammatory properties of the glucocorticoids to be used without fear of elevating intraocular pressure. A formulation containing tetrahydrocortexolone and dexamethasone is given.

ST glucocorticoid angiostatic steroid antiinflammatory ophthalmic; hydrocortexolone dexamethasone antiinflammatory ophthalmic

IT Inflammation inhibitors
(glucocorticoid-angiostatic steroid combinations, for ophthalmic pharmaceuticals)

IT Steroids, compounds
RL: BIOL (Biological study)
(mixts. with glucocorticoids, angiostatic, for antiinflammatory ophthalmic pharmaceutical)

IT Corticosteroids, compounds
RL: BIOL (Biological study)
(gluco-, mixts. with angiostatic steroid for antiinflammatory ophthalmic pharmaceutical)

IT Pharmaceutical dosage forms
(ophthalmic, of glucocorticoid and angiostatic steroid, for inflammation treatment)

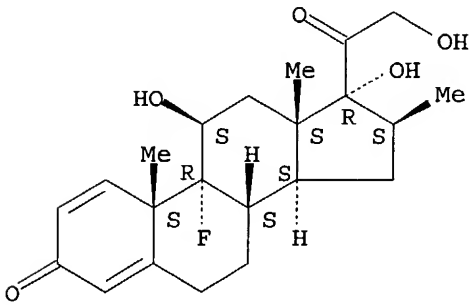
IT 50-02-2D, Dexamethasone, mixts. with angiostatic steroids 50-23-7D, Hydrocortisone, mixts. with angiostatic steroids 50-24-8D, Prednisolone, mixts. with angiostatic steroids 53-03-2D, Prednisone, mixts. with angiostatic steroids 68-60-0D, Tetrahydrocortexolone, mixts. with glucocorticoids 124-94-7D, Triamcinolone, mixts. with angiostatic steroids **378-44-9D**, Betamethasone, mixts. with angiostatic steroids 426-13-1D, Fluorometholone, mixts. with angiostatic steroids 2668-66-8D, Medrysone, mixts. with angiostatic steroids **10184-70-0D**, mixts. with glucocorticoids 105384-40-5D, mixts. with glucocorticoids 136305-04-9
RL: BIOL (Biological study)
(anti-inflammatory ophthalmic pharmaceuticals containing)

IT **378-44-9D**, Betamethasone, mixts. with angiostatic steroids **10184-70-0D**, mixts. with glucocorticoids
RL: BIOL (Biological study)
(anti-inflammatory ophthalmic pharmaceuticals containing)

RN 378-44-9 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17,21-trihydroxy-16-methyl-, (11β,16β)- (9CI) (CA INDEX NAME)

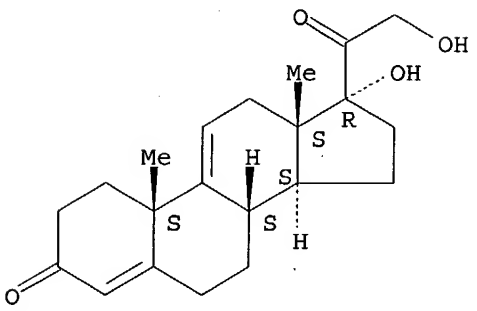
Absolute stereochemistry.



RN 10184-70-0 HCAPLUS

CN Pregna-4,9(11)-diene-3,20-dione, 17,21-dihydroxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 14 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1990:172351 HCAPLUS
DN 112:172351
ED Entered STN: 12 May 1990
TI Methods for controlling ocular hypertension with angiostatic steroids
IN Clark, Abbot F.
PA **Alcon Laboratories, Inc., USA**
SO U.S., 7 pp.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-56
ICS A61K031-58
NCL 514179000
CC 1-12 (Pharmacology)
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 4876250	A	19891024	US 1988-264918	19881031	<--
	AU 8943702	A1	19900503	AU 1989-43702	19891024	<--
	AU 628874	B2	19920924			
	CA 2001936	AA	19900430	CA 1989-2001936	19891031	<--
	CA 2001936	C	20000425			
	DK 8905429	A	19900501	DK 1989-5429	19891031	<--
	DK 172058	B1	19971006			
	EP 371617	A2	19900606	EP 1989-311238	19891031	<--
	EP 371617	A3	19920122			
	EP 371617	B1	19940608			
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE					
	JP 02196722	A2	19900803	JP 1989-285990	19891031	<--
	JP 3049504	B2	20000605			
	AT 106731	E	19940615	AT 1989-311238	19891031	<--
	US 5371078	A	19941206	US 1992-941485	19920908	<--
	US 5407926	A	19950418	US 1992-966118	19921023	<--
	US 5698545	A	19971216	US 1996-643387	19960506	<--
	US 5990099	A	19991123	US 1997-994114	19971219	<--
	WO 9903503	A1	19990128	WO 1998-US12711	19980618	<--
	W: AU, BR, CA, JP, MX, US					
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	AU 9881515	A1	19990210	AU 1998-81515	19980618	<--
	AU 734195	B2	20010607			
	EP 1003553	A1	20000531	EP 1998-931367	19980618	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
	BR 9811012	A	20001017	BR 1998-11012	19980618	<--
	JP 2001510170	T2	20010731	JP 2000-502798	19980618	<--

	MX 9911140	A	20000430	MX 1999-11140	19991202 <--
PRAI	US 1987-139222	B1	19871229 <--		
	US 1988-264918	A	19881031 <--		
	US 1989-399351	A2	19890828 <--		
	US 1989-419226	B2	19891010 <--		
	EP 1989-311238	A	19891031 <--		
	US 1990-555692	B1	19900723 <--		
	US 1990-559123	B2	19900727 <--		
	US 1992-941485	A1	19920908 <--		
	US 1994-349342	B1	19941202 <--		
	US 1996-643387	A1	19960506 <--		
	US 1997-895184	A	19970716 <--		
	US 1997-990424	B2	19971215 <--		
	WO 1998-US12711	W	19980618 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 4876250	ICM	A61K031-56
	ICS	A61K031-58
	NCL	514179000
US 5371078	ECLA	A61K031/56; C07J041/00B; C07J041/00B4; C07J051/00; A61K031/565; A61K031/565; A61K031/565T10; A61K031/57; A61K031/57L5; A61K031/58; A61K031/58; A61K031/665; C07J003/00; C07J005/00C1; C07J009/00; C07J011/00 <--
US 5407926	ECLA	A61K031/565; C07J011/00; C07J041/00B; C07J041/00B4; C07J051/00; A61K031/565; A61K031/565T10; A61K031/57; A61K031/57L5; A61K031/58; A61K031/58; A61K031/665; C07J003/00; C07J005/00C1; C07J009/00 <--
US 5698545	ECLA	A61K031/565; A61K031/565; A61K031/565T10; A61K031/58; A61K031/665; C07J003/00; C07J005/00C1; C07J009/00; C07J011/00; C07J041/00B; C07J041/00B4; C07J051/00; A61K031/57; A61K031/57L5; A61K031/58 <--
US 5990099	ECLA	A61K031/56; A61K031/565; A61K031/565; A61K031/565T10; A61K031/57; A61K031/57L5; A61K031/58; A61K031/58; A61K031/665; C07J003/00; C07J005/00C1; C07J009/00; C07J011/00; C07J041/00B; C07J041/00B4; C07J051/00 <--

OS MARPAT 112:172351

AB Ocular hypertension including that associated with primary open angle glaucoma are treated topically with the steroids tetrahydrocortexolone (THS), 4,9(11)-pregnadiene-17α,21-diol-3,20-dione, 6α-fluoro-17α,21-dihydroxy-16β-methylpregna-4,9(11)-diene-3,20-dione, and their pharmaceutically acceptable salts. These steroids may act by inhibiting the accumulation or stimulating the dissoln. of amorphous extracellular material in the trabecular meshwork of the eye. THS lowered intraocular pressure in rabbits with steroid-induced ocular hypertension.

ST eye hypertension treatment angiostatic steroid

IT **Glaucoma (disease)**
(angiostatic steroids for treatment of)

IT Steroids, biological studies
RL: BIOL (Biological study)
(angiostatic, in glaucoma treatment)

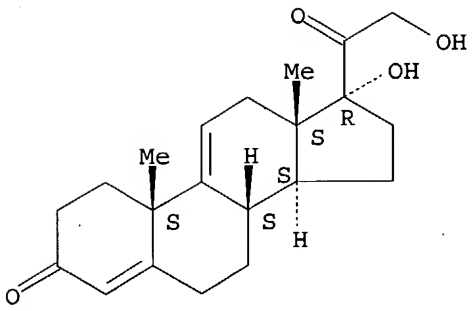
IT 68-60-0, Tetrahydrocortexolone **10184-70-0** 105384-40-5
RL: BIOL (Biological study)
(glaucoma treatment with)

IT **10184-70-0**
RL: BIOL (Biological study)
(glaucoma treatment with)

RN 10184-70-0 HCAPLUS

CN Pregna-4,9(11)-diene-3,20-dione, 17,21-dihydroxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



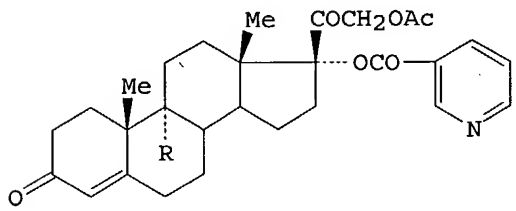
L44 ANSWER 15 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1989:135568 HCAPLUS
DN 110:135568
ED Entered STN: 15 Apr 1989
TI Selective chlorination of steroids and other substrates directed by covalently linked agents comprising nitrogen-containing rings acting as templates
IN Breslow, Ronald; Brandl, Michael; Adam, Alan D.; Hunger, Jurgen
PA Columbia University, USA
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07J043-00
ICS C07J009-00; C07J001-00
CC 32-7 (Steroids)
Section cross-reference(s): 21
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8809337	A1	19881201	WO 1988-US1774	19880526 <--
	W: AU, DK, JP				
	RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	US 4920216	A	19900424	US 1987-55139	19870528 <--
	AU 8819459	A1	19881221	AU 1988-19459	19880526 <--
PRAI	US 1987-55139		19870528 <--		
	WO 1988-US1774		19880526 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 8809337	ICM	C07J043-00
	ICS	C07J009-00; C07J001-00

OS CASREACT 110:135568; MARPAT 110:135568
GI



I

AB Hydroxy steroids were chlorinated at various ring H positions by esterifying with N-containing heterocyclic acids, which then act as templates

for regioselective chlorination by various agents. Esterification of cortexolone 21-acetate by nicotinic anhydride in MeOCH2CH2OMe containing 4-(dimethylamino)pyridine gave 97% of the 21-acetate 17α-nicotinate I (R = H). This compound was chlorinated by 2.0 equiv SO2Cl2 and 0.2 equiv AIBN in CH2Cl2 under irradiation at 25° to give 100% crude I (R = Cl) containing approx. 10% I (R = H). Dehydrochlorination of I (R = Cl) using AgBF4 in Me2CO gave the Δ4,9(11) diene, 100% as crude and 70% after chromatog.

ST chlorination steroid nitrogen template; nicotinate cholestanol cortexolone template chlorination

IT Templates
(nitrogen-containing heterocyclic esters, for chlorination of hydroxy steroids and other compds.)

IT Dehydrogenation
(of steroids and other compds., via regioselective template chlorination and dehydrochlorination)

IT Dehydrochlorination
(regioselective template chlorination and, of steroids and other compds.)

IT Steroids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(regioselective template chlorination of, via nitrogen-containing heterocyclic esters)

IT Steroids, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(chloro, preparation of, via regioselective template chlorination using nitrogen-containing heterocyclic esters)

IT Chlorination
(template, regioselective, of steroids and other compds., via esters with nitrogen-containing heterocyclic acids)

IT 7647-01-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(dehydrochlorination, regioselective template chlorination and, of steroids and other compds.)

IT 1333-74-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(dehydrogenation, of steroids and other compds., via regioselective template chlorination and dehydrochlorination)

IT 516-95-0, 3α-Cholestanol
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of, with carbonyldiimidazole)

IT 530-62-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of, with cholestanol)

IT 16837-38-0, Nicotinic anhydride
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of, with hydroxy steroids)

IT 640-87-9 24510-54-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of, with nicotinic anhydride)

IT 108674-98-2P 119669-98-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and dehydrochlorination of)

IT 108665-15-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and dehydrochlorination, hydrolysis, and acetylation of)

IT 119669-94-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis and acetylation of)

IT 101836-12-8P 119669-90-8P 119669-91-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(preparation and hydrolysis-dehydrochlorination of)

IT 119669-99-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and methanolysis of)

IT 108665-13-0P 119669-89-5P 119669-97-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and regioselective template chlorination of)

IT **7753-60-8P** 13209-41-1P 37772-32-0P 119669-92-0P
119669-93-1P 119669-95-3P 119669-96-4P 119670-00-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, via regioselective template chlorination)

IT 50-02-2DP, Dexamethasone, dehydro derivs. 50-24-8DP, dehydro derivs. 124-94-7DP, Triamcinolone, dehydro derivs. **378-44-9DP**, dehydro derivs.
RL: PREP (Preparation)
(production of, via regioselective template chlorination and dehydrochlorination)

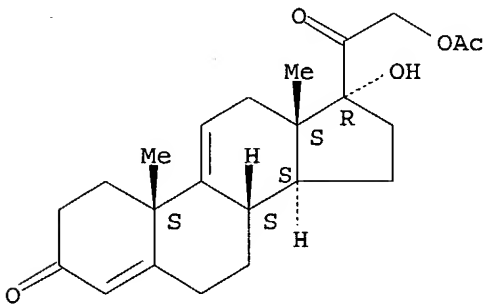
IT 932-72-9 7782-50-5, Chlorine, reactions 7791-25-5, Sulfuryl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(regioselective template chlorination by, of steroids and other organic compds.)

IT 152-58-9 101836-11-7 108665-12-9 108665-14-1 119669-85-1 119669-86-2 119669-87-3 119669-88-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(regioselective template chlorination of)

IT **7753-60-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, via regioselective template chlorination)

RN 7753-60-8 HCAPLUS
CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

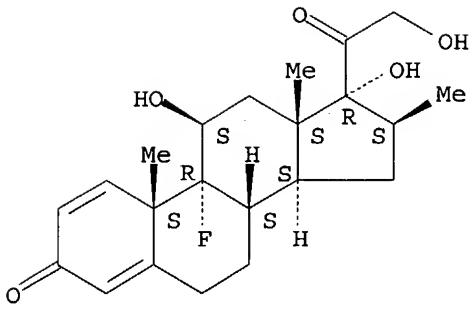
Absolute stereochemistry.



IT **378-44-9DP**, dehydro derivs.
RL: PREP (Preparation)
(production of, via regioselective template chlorination and dehydrochlorination)

RN 378-44-9 HCAPLUS
CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17,21-trihydroxy-16-methyl-, (11β,16β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 16 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1984:190328 HCAPLUS
DN 100:190328
ED Entered STN: 08 Jun 1984
TI Conversion of 1,2-saturated 3-ketosteroids to 1,2-dehydrosteroids
IN Kominek, Leo Alyosius; Wolf, Holly Jo; Evans, Timothy Wendell
PA Upjohn Co., USA
SO Ger. Offen., 34 pp.
CODEN: GWXXBX
DT Patent
LA German
IC C07J007-00; C07J001-00; C07J005-00; C12P033-02
CC 16-2 (Fermentation and Bioindustrial Chemistry)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	DE 3322120	A1	19840202	DE 1983-3322120	19830620	<--
	DE 3322120	C2	19921008			
	US 4524134	A	19850618	US 1982-436552	19821025	<--
	HU 31767	O	19840528	HU 1983-2300	19830624	<--
	HU 196464	B	19881128			
	HU 196847	B	19890130	HU 1983-2671	19830624	<--
	GB 2123833	A1	19840208	GB 1983-17422	19830627	<--
	GB 2123833	B2	19860611			
	CH 657871	A	19860930	CH 1983-3784	19830708	<--
	DD 213242	A5	19840905	DD 1983-253123	19830715	<--
	NL 8302596	A	19840216	NL 1983-2596	19830720	<--
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	FR 2531101	A1	19840203	FR 1983-12564	19830729	<--
	FR 2531101	B1	19851115			
	GB 2131811	A1	19840627	GB 1984-2640	19840201	<--
	GB 2131811	B2	19860611			
	US 4704358	A	19871103	US 1985-721011	19850408	<--
	US 4684610	A	19870804	US 1985-724036	19850417	<--
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PRAI	US 1982-403949		19820730	<--		
	US 1982-436552		19821025	<--		
	US 1983-475437		19830315	<--		
	GB 1983-17422		19830627	<--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
DE 3322120	IC	C07J007-00IC C07J001-00IC C07J005-00IC C12P033-02

OS CASREACT 100:190328

AB Steroids are desatd. in the 1,2-position with dried cells of Arthrobacter simplex or Bacterium cyclooxidans in the presence of an exogenous electron carrier. Thus, 0.5 g of B. cyclooxidans ATCC 12673 cells that had been vacuum dried at 45° was added to 50 mL of 50 mM pH 7.5 phosphate buffer. Then 0.25 mL of an EtOH solution of menadione [58-27-5] (8.6 mg menadione/mL EtOH) was added and a 10% solution of 6α-methylhydrocortisone (I) [1625-39-4] in DMF was added to a final concentration of 0.5 g/L. After shaking for 4 h at 28°, the transformation of I to 6α-methylprednisolone [83-43-2] was 91%. The presence of a water-immiscible aromatic hydrocarbon increased the yield still more.

ST steroid desatn Arthrobacter Bacterium

IT Steroids, preparation
RL: PREP (Preparation)
(1,2-dehydro-3-keto, by microbial action)

IT Arthrobacter simplex
Bacterium cyclooxydans
(dried, steroid desatn. with)

IT Ubiquinones
RL: BIOL (Biological study)
(in steroid 1,2-desatn. with bacteria)

IT 50-23-7 63-05-8 382-44-5 382-45-6 433-82-9 434-03-7 564-33-0
1035-69-4 1058-55-5 1176-81-4 1549-35-5 1625-39-4 2285-45-2
2358-07-8 2395-17-7 2586-44-9 3386-04-7 3494-53-9 3932-49-8
5327-59-3 **7753-60-8** 18762-16-8 18762-17-9 18769-18-1
23460-76-6 24510-87-0 25092-31-3 34542-56-8 39780-54-6
73553-82-9 74220-43-2 74915-67-6 85764-25-6 90039-83-1
90039-84-2 90039-85-3 90039-86-4 90039-87-5 90039-88-6
90081-44-0
RL: BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(1,2-desatn. of, bacterial)

IT 42613-28-5
RL: BIOL (Biological study)
(bacteria cells containing, steroid desatn. with)

IT 58-27-5 71-43-2, biological studies 108-88-3, biological studies
130-15-4 130-36-9 299-11-6 956-48-9 1330-20-7, biological studies
12001-79-5
RL: BIOL (Biological study)
(in steroid 1,2-desatn. with bacteria)

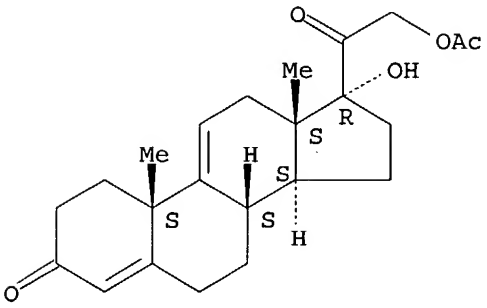
IT 50-24-8P 53-34-9P 67-73-2P 83-43-2P 124-94-7P 152-97-6P
356-12-7P **378-44-9P** 570-36-5P 806-29-1P 897-06-3P
898-84-0P 910-99-6P 912-38-9P 981-34-0P 987-24-6P 1176-82-5P
2476-74-6P 2597-76-4P 2823-42-9P 3859-65-2P 3870-07-3P
3937-70-0P 4380-55-6P 6598-95-4P 7738-93-4P 7801-18-5P
10106-41-9P 10184-69-7P 13209-41-1P 13504-15-9P 13889-22-0P
15375-21-0P 18769-24-9P 25092-32-4P 37413-91-5P 39672-76-9P
39780-55-7P 51166-61-1P 51259-83-7P 61919-52-6P 74410-22-3P
77017-20-0P 83509-37-9P 90039-89-7P 90039-90-0P 90039-91-1P
90039-92-2P 90039-93-3P 90039-94-4P 90039-95-5P 90039-96-6P
90039-97-7P 90039-98-8P 90063-31-3P
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(manufacture of, microbial)

IT **7753-60-8**
RL: BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(1,2-desatn. of, bacterial)

RN 7753-60-8 HCAPLUS

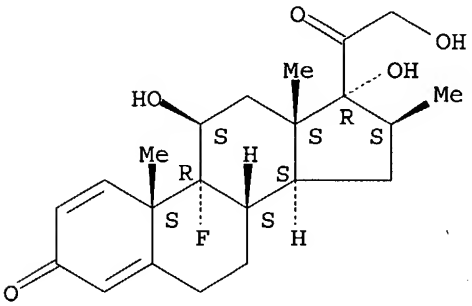
CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **378-44-9P**
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(manufacture of, microbial)
RN 378-44-9 HCAPLUS
CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17,21-trihydroxy-16-methyl-, (11β,16β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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L40 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:270085 HCAPLUS
DN 140:297513
ED Entered STN: 02 Apr 2004
TI Method using immunophilin-binding compounds for inhibiting choroidal neovascularization, animal model, and screening method
IN Laties, Alan; Wen, Rong; Lou, Zhijun
PA Trustees of the University of Pennsylvania, USA
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N
CC 1-8 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004027027	A2	20040401	WO 2003-US29188	20030918
	WO 2004027027	A3	20040521		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-412088P P 20020918

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004027027	ICM	C12N

AB The invention discloses compns. and methods for inhibiting unwanted angiogenesis, particularly those of ocular tissues. The treatment, inhibition, and/or prevention of choroidal neovasculature (CNV) is provided, along with an animal model for CNV and imaging techniques that permit the screening of potential agents as anti-angiogenesis and anti-CNV agents. The methodol. of the invention uses immunophilin-binding compds., e.g. rapamycin.

ST immunophilin binding compd choroidal neovascularization inhibition; drug screening animal model choroidal neovascularization

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NF-κB (nuclear factor of κ light chain gene enhancer in B-cells), inhibitors; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, screening method, and use with other agents)

IT Eye, disease
(angioid streaks; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)

IT Integrins
Vitronectin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; immunophilin-binding compds. for inhibiting choroidal neovasculárization, animal model, screening method, and use with other agents)

IT Metals, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coordination; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, screening method, and use with other agents)

IT Peptides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclic; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, screening method, and use with other agents)

IT Eye, disease
(diabetic retinopathy; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)

IT Angiogenesis inhibitors
Disease models
Drug delivery systems
Drug screening
Human
(immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)

IT Immunophilins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(immunophilin-binding compds. for inhibiting choroidal

neovascularization, animal model, and screening method)
IT Collagens, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
IT Drug targets
Photosensitizers (pharmaceutical)
(immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, screening method, and use with other agents)
IT Antibodies and Immunoglobulins
Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, screening method, and use with other agents)
IT Vision
(improvement; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
IT Drug delivery systems
(injections; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
IT Dyes
(lipophilic; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
IT **Eye, disease**
(**macula, degeneration**; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
IT **Eye, disease**
(**macula, senile degeneration**; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
IT **Eye, disease**
(myopic **degeneration**; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
IT Angiogenesis
(neovascularization, retinal; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
IT Eye, disease
(ocular trauma; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
IT Drug delivery systems
(ophthalmic; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
IT Drug delivery systems
(oral; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
IT Drug delivery systems
(parenterals; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
IT Ion channel blockers
(potassium; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, screening method, and use with other agents)
IT Histoplasma capsulatum
(presumed ocular histoplasmosis syndrome; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)

IT Eye, disease
(retina, neovascularization; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
IT Drug delivery systems
(topical; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
IT Blood vessel
(visualization; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(αvβ1, antagonists; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, screening method, and use with other agents)
IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(αvβ3, antagonists; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, screening method, and use with other agents)
IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(γ; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, screening method, and use with other agents)
IT 30525-89-4, Paraformaldehyde 119978-18-6, Matrigel
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
IT 53123-88-9, Rapamycin 53123-88-9D, Rapamycin, analogs 104987-11-3, Tacrolimus
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, and screening method)
IT 64-86-8, Colchicine 124-94-7, Triamcinolone 145-63-1D, Suramin, analogs 154-42-7D, 6-Thioguanine, analogs 362-07-2, 2-Methoxyestradiol 989-51-5, Epigallocatechin-3-gallate 2295-31-0D, Thiazolidinedione, derivs. 4759-48-2, Accutane 6493-05-6, Pentoxifylline **7753-60-8**, **Anecortave acetate** 9027-98-9, Arginine deiminase 15307-86-5, Diclofenac 16330-92-0 19171-19-8 23110-15-8, Fumagillin 25769-03-3, 1-Pyrrolidinecarbodithioic acid 78281-72-8, Nepafenac 82834-16-0, Perindopril 85441-61-8, Quinapril 86090-08-6, Angiostatin 97322-87-7, Troglitazone 122320-73-4, Rosiglitazone 127064-91-9, ANO 2 129298-91-5D, TNP 470, analogs 129497-78-5, Visudyne 145599-86-6, Cerivastatin 148717-90-2, Squalamine 162011-90-7, Rofecoxib 179324-69-7, Velcade 187888-07-9, Endostatin 197980-93-1, Pigment epithelium-derived factor 207692-22-6, AMG 1470 222716-86-1, Macugen 347396-82-1, Ranibizumab 675623-65-1, Endorepellin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, screening method, and use with other agents)
IT 9004-54-0, Dextran, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, screening method, and use with other agents)
IT 9000-81-1, Acetylcholinesterase 9015-82-1, Angiotensin-converting enzyme

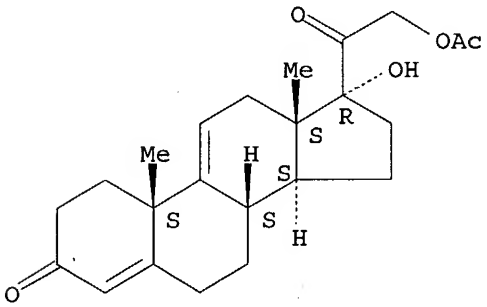
39391-18-9, Cyclooxygenase 140879-24-9, Proteasome 141436-78-4, Protein kinase C 148047-29-4, Tie-2 kinase 151769-13-0, Tie1 receptor tyrosine kinase 171715-28-9, Mammalian target of rapamycin 175449-82-8, Collagenase 3 386705-49-3, Vascular endothelial growth factor receptor kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, screening method, and use with other agents)

IT 9028-02-8, Transfer RNA synthetase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (modulators; immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, screening method, and use with other agents)

IT **7753-60-8, Anecortave acetate**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunophilin-binding compds. for inhibiting choroidal neovascularization, animal model, screening method, and use with other agents)

RN 7753-60-8 HCAPLUS
CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:120728 HCAPLUS
DN 140:157931
ED Entered STN: 13 Feb 2004
TI Protection of visual acuity in patients with age related **macular degeneration** by administration of **anecortave acetate**
IN **Jerdan, Janice A.; Zilliox, Patricia; Robertson, Stella M.**
PA **Alcon, Inc., Switz.**
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-56
CC 2-4 (Mammalian Hormones)
Section cross-reference(s): 1
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004012742	A1	20040212	WO 2003-US20154	20030626 <--

W: AU, BR, CA, CN, JP, KR, MX, PH, PL, RU, US, ZA
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,

IT, LU, MC, NL, PT, RO, SE, SI, SK, TR
US 2004127472 A1 20040701 US 2003-606501 20030626 <--
PRAI US 2002-401220P P 20020805 <--
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004012742	ICM	A61K031-56

AB The invention discloses the use of anercortave acetate or the alc. thereof for the protection of visual acuity in patients with age related **macular degeneration.**

ST **anecortave acetate** vision acuity age related **macular degeneration**

IT **Eye, disease**
(**macula, senile degeneration**; protection of visual acuity in patients with age related **macular degeneration** by administration of **anecortave acetate**)

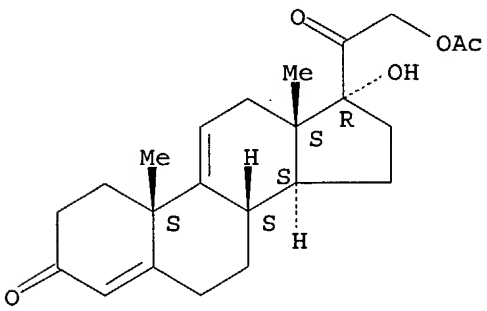
IT Drug delivery systems
Human
Vision
(protection of visual acuity in patients with age related **macular degeneration** by administration of **anecortave acetate**)

IT **7753-60-8, Anecortave acetate**
10184-70-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protection of visual acuity in patients with age related **macular degeneration** by administration of **anecortave acetate**)

IT **7753-60-8, Anecortave acetate**
10184-70-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protection of visual acuity in patients with age related **macular degeneration** by administration of **anecortave acetate**)

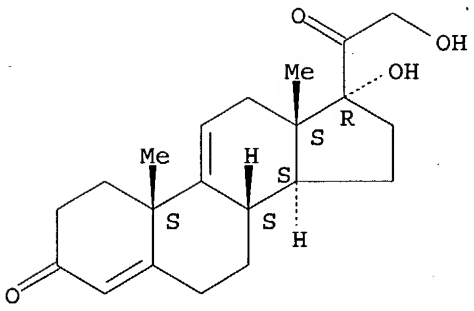
RN 7753-60-8 HCAPLUS
CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 10184-70-0 HCAPLUS
CN Pregna-4,9(11)-diene-3,20-dione, 17,21-dihydroxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:153653 HCAPLUS
DN 139:53197
ED Entered STN: 28 Feb 2003
TI **Anecortave acetate**: Treatment of age-related **macular degeneration** angiogenesis inhibitor
AU Sorbera, L. A.; Leeson, P. A.; Castaner, J.; Bayes, M.
CS Prous Science, Barcelona, 08080, Spain
SO Drugs of the Future (**2002**), 27(11), 1039-1048
CODEN: DRFUD4; ISSN: 0377-8282
PB Prous Science
DT Journal; General Review
LA English
CC 32-0 (Steroids)
Section cross-reference(s): 1
AB A review was presented of syntheses and pharmacol. of **anecortave acetate.** Angiogenesis is a normal process that is strictly controlled. If this fine control is disrupted, chronic activation can occur resulting in inappropriate tissue responses that can lead to pathol. neovascularization. Many chronic ocular diseases are due to chronic stimulation of angiogenesis and they are the major cause of blindness worldwide. Treatment for these ocular neovascular disorders should involve delay, arrest or prevention of new capillary proliferation with the absence of or the presence of only minimal adverse events. To date, surgery, laser photocoagulation and glucocorticoid therapy are the usual treatment options. However, they may be ineffective, worsen the condition or, in the case of glucocorticoids, be associated with steroid-induced adverse events. Several classes of antiangiogenic agents have been described and they include antibiotics, polypeptides, polycations, polyanions, steroids, VEGF antagonists and integrin antagonists. Angiostatic steroids in particular have been shown to inhibit angiogenesis without the typical steroid activity that is associated with side effects. One such novel angiostatic steroid chosen for further development is **anecortave acetate.** It has shown excellent preclin. antiangiogenic efficacy and promising clin. activity as a treatment for ocular neovascular disorders.
ST review **anecortave acetate** angiogenesis inhibitor neovascularization eye disease; **macular degeneration** angiogenesis inhibitor **anecortave acetate** review
IT **Eye, disease**
(**macula, senile degeneration**, treatment; review was presented of syntheses and pharmacol. of **anecortave acetate**, an age-related **macular degeneration** angiogenesis inhibitor)
IT Angiogenesis inhibitors
(review was presented of syntheses and pharmacol. of **anecortave acetate**, an age-related **macular degeneration** angiogenesis inhibitor)

IT **7753-60-8P, Anecortave acetate**
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(review was presented of syntheses and pharmacol. of **anecortave acetate**, an age-related **macular degeneration** angiogenesis inhibitor)

RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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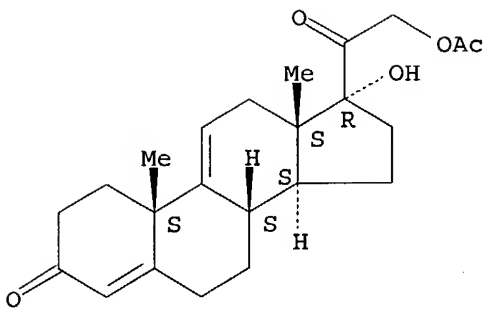
IT **7753-60-8P, Anecortave acetate**
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(review was presented of syntheses and pharmacol. of **anecortave acetate**, an age-related **macular degeneration** angiogenesis inhibitor)

RN 7753-60-8 HCAPLUS

CN Pregna-4,9(11)-diene-3,20-dione, 21-(acetyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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FILE COVERS 1974 TO 26 Aug 2004 (20040826/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all tot l59

L59 ANSWER 1 OF 6 EMBASE
on STN
AN 2003072455 EMBASE
TI **Anecortave acetate**: Treatment of age-related **macular degeneration** angiogenesis inhibitor.
AU Sobrera L.A.; Leeson P.A.; Castaner J.; Bayes M.
CS L.A. Sobrera, Prous Science, P.O. Box 540, 08080 Barcelona, Spain
SO Drugs of the Future, (1 Nov 2002) 27/11 (1039-1048).
Refs: 42
ISSN: 0377-8282 CODEN: DRFUD4
CY Spain
DT Journal; Article
FS 030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB Angiogenesis is a normal process that is strictly controlled. If this fine control is disrupted, chronic activation can occur resulting in inappropriate tissue responses that can lead to pathologic neovascularization. Many chronic ocular diseases are due to chronic stimulation of angiogenesis and they are the major cause of blindness worldwide. Treatment for these ocular neovascular disorders should involve delay, arrest or prevention of new capillary proliferation with the absence of or the presence of only minimal adverse events. To date, surgery, laser photocoagulation and glucocorticoid therapy are the usual treatment options. However, they may be ineffective, worsen the condition or, in the case of glucocorticoids, be associated with steroid-induced adverse events. Several classes of antiangiogenic agents have been described and they include antibiotics, polypeptides, polycations, polyanions, steroids, VEGF antagonists and integrin antagonists. Angiostatic steroids in particular have been shown to inhibit angiogenesis without the typical steroid activity that is associated with side effects. One such novel angiostatic steroid chosen for further development is **anecortave acetate.** It has shown excellent preclinical antiangiogenic efficacy and promising clinical activity as a treatment for

ocular neovascular disorders.
CT Medical Descriptors:
***retina macula age related degeneration: DT, drug therapy**
***retina macula age related degeneration: TH, therapy**
laser coagulation
angiogenesis
retina neovascularization: CO, complication
retina neovascularization: DT, drug therapy
retina neovascularization: TH, therapy
blindness: CO, complication
corticosteroid therapy
drug efficacy
drug activity
drug synthesis
drug structure
drug mechanism
animal model
drug safety
article
Drug Descriptors:
*angiogenesis inhibitor: AN, drug analysis
*angiogenesis inhibitor: DV, drug development
*angiogenesis inhibitor: DT, drug therapy
*angiogenesis inhibitor: PD, pharmacology
*steroid: AN, drug analysis
*steroid: DV, drug development
*steroid: DT, drug therapy
*steroid: PD, pharmacology
***anecortave: AN, drug analysis**
***anecortave: DV, drug development**
***anecortave: DO, drug dose**
***anecortave: DT, drug therapy**
***anecortave: PD, pharmacology**
antibiotic agent: DT, drug therapy
polypeptide: DT, drug therapy
polycation: DT, drug therapy
polyanion: DT, drug therapy
vasculotropin inhibitor: DT, drug therapy
integrin
integrin antagonist: DT, drug therapy
urokinase
stromelysin
plasminogen activator inhibitor 1
unclassified drug
RN (**anecortave**) **7753-60-8**; (urokinase) 139639-24-0;
(stromelysin) 79955-99-0; (plasminogen activator inhibitor 1) 140208-23-7
CN **(1) Al 3789**
CO (1) Alcon (United States)

L59 ANSWER 2 OF 6 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
AN 2003034758 EMBASE
TI New treatments for CNV secondary to AMD: What evidence exists to support a
treatment recommendation?.
AU Lanzetta P.
CS P. Lanzetta, Department of Ophthalmology, University of Udine, Viale
Venezia 410, 33100 Udine, Italy. paolo.lanzetta@dsc.uniud.it
SO Graefe's Archive for Clinical and Experimental Ophthalmology, (2002)
240/11 (885-888).
Refs: 34
ISSN: 0721-832X CODEN: GACODL
CY Germany
DT Journal; Editorial

FS 012 Ophthalmology
017 Public Health, Social Medicine and Epidemiology
030 Pharmacology
036 Health Policy, Economics and Management
037 Drug Literature Index
LA English
CT Medical Descriptors:
***subretinal neovascularization: CO, complication**
***subretinal neovascularization: DM, disease management**
***subretinal neovascularization: DT, drug therapy**
***subretinal neovascularization: RT, radiotherapy**
***subretinal neovascularization: SU, surgery**
***subretinal neovascularization: TH, therapy**
retina macula age related degeneration: DT, drug therapy
eye disease: CO, complication
eye disease: DM, disease management
eye disease: DT, drug therapy
eye disease: RT, radiotherapy
eye disease: SU, surgery
eye disease: TH, therapy
visual impairment: CO, complication
quality of life
laser coagulation
photodynamic therapy
hyperthermic therapy
retina macula translocation
drug efficacy
disease severity
drug safety
risk assessment
visual acuity
treatment outcome
long term care
gene therapy
prognosis
health care quality
medical care
patient care
human
clinical trial
adult
editorial
priority journal
Drug Descriptors:
angiogenesis inhibitor: CT, clinical trial
angiogenesis inhibitor: DT, drug therapy
angiogenesis inhibitor: PD, pharmacology
benzoporphyrin derivative: CT, clinical trial
benzoporphyrin derivative: DT, drug therapy
benzoporphyrin derivative: PD, pharmacology
antioxidant: CB, drug combination
antioxidant: DT, drug therapy
antioxidant: PO, oral drug administration
zinc derivative: CB, drug combination
zinc derivative: DT, drug therapy
zinc derivative: PO, oral drug administration
placebo
tin ethyl etiopurpurin: CT, clinical trial
tin ethyl etiopurpurin: DT, drug therapy
tin ethyl etiopurpurin: PD, pharmacology
photosensitizing agent: CT, clinical trial
photosensitizing agent: DT, drug therapy
photosensitizing agent: PD, pharmacology

indocyanine green
interferon: CT, clinical trial
interferon: DT, drug therapy
interferon: PD, pharmacology
matrix metalloproteinase inhibitor: CT, clinical trial
matrix metalloproteinase inhibitor: DT, drug therapy
matrix metalloproteinase inhibitor: PD, pharmacology
prinomastat: CT, clinical trial
prinomastat: DT, drug therapy
prinomastat: PD, pharmacology
vasculotropin inhibitor: CT, clinical trial
vasculotropin inhibitor: DT, drug therapy
vasculotropin inhibitor: PD, pharmacology
aptamer
rhufab v2: CT, clinical trial
rhufab v2: DT, drug therapy
vasculotropin antibody: CT, clinical trial
vasculotropin antibody: DT, drug therapy
anecortave: CT, clinical trial
anecortave: DT, drug therapy
anecortave: PD, pharmacology
steroid: CT, clinical trial
steroid: DT, drug therapy
steroid: PD, pharmacology
alpha tocopherol: CB, drug combination
alpha tocopherol: DT, drug therapy
alpha tocopherol: PO, oral drug administration
beta carotene: CB, drug combination
beta carotene: DT, drug therapy
beta carotene: PO, oral drug administration
zinc oxide: CB, drug combination
zinc oxide: DT, drug therapy
zinc oxide: PO, oral drug administration
cupric oxide: CB, drug combination
cupric oxide: DT, drug therapy
cupric oxide: PO, oral drug administration
copper derivative: CB, drug combination
copper derivative: DT, drug therapy
copper derivative: PO, oral drug administration
unclassified drug

RN (benzoporphyrin derivative) 113719-89-4; (indocyanine green) 3599-32-4; (prinomastat) 192329-42-3, 195008-93-6; (**anecortave**) **7753-60-8**; (alpha tocopherol) 1406-18-4, 1406-70-8, 52225-20-4, 58-95-7, 59-02-9; (beta carotene) 7235-40-7; (zinc oxide) 1314-13-2; (cupric oxide) 1317-38-0
CN (1) Visudyne; Ag 3340
CO (1) Novartis

L59 ANSWER 3 OF 6 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 2001050805 EMBASE
TI IBC's 6th annual conference on angiogenesis: Novel therapeutic developments.
AU Mousa S.A.
CS S.A. Mousa, DuPont Pharmaceuticals Co., Wilmington, DE, United States
SO Expert Opinion on Investigational Drugs, (2001) 10/2 (387-391). ISSN: 1354-3784 CODEN: EOIDER
CY United Kingdom
DT Journal; Article
FS 005 General Pathology and Pathological Anatomy
012 Ophthalmology
014 Radiology
016 Cancer

037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB Angiogenesis is a process that is dependent upon co-ordinate production of angiogenesis stimulatory and inhibitory (angiostatic) molecules. Any imbalance in this regulatory circuit may lead to the development of a number of angiogenesis-mediated diseases. Angiogenesis is a multi-step process including activation, adhesion, migration, proliferation and transmigration of endothelial cells across cell matrices to or from new capillaries and from existing vessels. Angiogenesis is a process involved in the formation of new vessels by sprouting from pre-existing vessels. In contrast, vessel rudiments are sorted by a process termed vasculogenesis. Endothelial heterogeneity and organ specificity might contribute to differences in the response to different anti-angiogenic mechanisms (cultured EC versus microvascular EC isolated from different tissues). Under normal physiological conditions in mature organisms, endothelial cell turnover or angiogenesis is extremely slow (from months to years). However, angiogenesis can be activated for a limited time in certain situations such as wound healing and ovulation. In certain pathological states, such as human metastasis (oncology) and ocular neovascularisation, disorders including diabetic retinopathy and age-related **macular degeneration** (ophthalmology), there is excessive and sustained angiogenesis. Hence, understanding the mechanisms involved in the regulation of angiogenesis could have a major impact in the prevention and treatment of pathological angiogenic processes. Additionally, endothelial cells play a major role in the modelling of blood vessels. The interplay of growth factors, cell adhesion molecules, matrix proteases and specific signal transduction pathways either in the maintenance of the quiescent state or in the reactivation of endothelial cells is critical in physiological and pathological angiogenic processes.
CT Medical Descriptors:
*angiogenesis
regulatory mechanism
disease course
endothelium cell
cell activation
cell adhesion
cell migration
cell proliferation
cell transfer
extracellular matrix
capillary
cell heterogeneity
cell culture
cell isolation
tissue
physiology
turnover time
wound healing
ovulation
pathology
metastasis
eye disease: DT, drug therapy
diabetic retinopathy
retina macula degeneration
ophthalmology
model
signal transduction
cancer therapy
protein domain
solid tumor: DT, drug therapy
side effect: SI, side effect

nuclear magnetic resonance imaging
human
nonhuman
rat
clinical trial
phase 1 clinical trial
phase 2 clinical trial
phase 3 clinical trial
controlled study
animal cell
article
Drug Descriptors:
*angiogenesis inhibitor: PD, pharmacology
angiogenic factor
cell adhesion molecule: EC, endogenous compound
growth factor: EC, endogenous compound
proteinase: EC, endogenous compound
heparin: CT, clinical trial
heparin: PD, pharmacology
anticoagulant agent: PD, pharmacology
low molecular weight heparin: PD, pharmacology
tinzaparin: CT, clinical trial
tinzaparin: DT, drug therapy
tinzaparin: PR, pharmaceutics
tinzaparin: PD, pharmacology
tissue factor pathway inhibitor: CT, clinical trial
tissue factor pathway inhibitor: PR, pharmaceutics
tissue factor pathway inhibitor: PD, pharmacology
kininostatin: AN, drug analysis
kininostatin: PD, pharmacology
high molecular weight kininogen: AN, drug analysis
high molecular weight kininogen: PD, pharmacology
vitronectin: EC, endogenous compound
monoclonal antibody: DV, drug development
monoclonal antibody: PD, pharmacology
collagen type 4: PD, pharmacology
imc 1c 11: CT, clinical trial
imc 1c 11: DV, drug development
imc 1c 11: PD, pharmacology
vasculotropin receptor: EC, endogenous compound
vasculotropin: EC, endogenous compound
vasculotropin antibody: CT, clinical trial
vasculotropin antibody: DT, drug therapy
matrix metalloproteinase inhibitor: CT, clinical trial
matrix metalloproteinase inhibitor: DT, drug therapy
matrix metalloproteinase inhibitor: PD, pharmacology
matrix metalloproteinase inhibitor: PO, oral drug administration
2 methoxyestradiol: CT, clinical trial
2 methoxyestradiol: TO, drug toxicity
2 methoxyestradiol: PD, pharmacology
2 methoxyestradiol: PO, oral drug administration
integrin: EC, endogenous compound
anecortave: AE, adverse drug reaction
anecortave: CT, clinical trial
anecortave: DT, drug therapy
anecortave: PD, pharmacology
unclassified drug

RN (proteinase) 9001-92-7; (heparin) 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5; (tissue factor pathway inhibitor) 116638-34-7; (high molecular weight kininogen) 97792-85-3; (vasculotropin) 127464-60-2; (2 methoxyestradiol) 362-07-2; (**anecortave**) **7753-60-8**

CN (1) Imc 1c 11; **(2) Al 3789**

CO (1) Imclone; (2) Alcon

L59 ANSWER 4 OF 6 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 2001029006 EMBASE
TI The effect of an angiostatic steroid on neovascularization in a rat model of retinopathy of prematurity.
AU Penn J.S.; Rajaratnam V.S.; Collier R.J.; Clark A.F.
CS J.S. Penn, Dept. of Ophthalmol. and Visual Sci., Vanderbilt Univ. School of Medicine, 8016 Medical Center East, 2115 21st Avenue South, Nashville, TN 37232-8808, United States. john.penn@mcmail.vanderbilt.edu
SO Investigative Ophthalmology and Visual Science, (2001) 42/1 (283-290). Refs: 57
ISSN: 0146-0404 CODEN: IOVSDA
CY United States
DT Journal; Article
FS 012 Ophthalmology
037 Drug Literature Index
LA English
SL English
AB Purpose. The inhibition of angiogenesis by angiostatic steroids has been demonstrated in a variety of systems, including rabbit and rat cornea. There is considerable interest in the therapeutic potential of this class of compounds for angiogenic ocular conditions such as diabetic retinopathy, **macular degeneration**, and retinopathy of prematurity (ROP). This study was designed to test the capacity of an angiostatic steroid, **anecortave acetate**, to inhibit retinal neovascularization using a rat model of ROP and to investigate the mechanism of the effect. Methods. At birth, rats were placed in an atmosphere of varying oxygen that produces retinal neovascular changes that approximate human ROP. The rats then received intravitreal injections of either **anecortave acetate** or vehicle at varying times, and all were subsequently placed in room air. Retinas were assessed for plasminogen activator inhibitor (PAI)-1 mRNA level by RNase protection assay at 1, 2, and 3 days after injection and for normal and abnormal blood vessel growth 3 days later. Results. A significant reduction in the severity of abnormal retinal neovascularization was observed in the steroid-treated eyes compared with vehicle-injected eyes in ROP rats, yet the extent of normal total retinal vascular area was not significantly different. The drug had no effect on either retinal vascular area or neovascularization when tested in room air-raised control rats. Drug-injected eyes demonstrated a six- to ninefold increase in PAI-1 mRNA at 1 to 3 days after injection. Conclusions. This study represents the first therapeutic effect of an angiostatic steroid in an animal model of neovascular retinopathy. Additionally, the induction of PAI-1 indicates a mechanism of action for this class of compounds, and this is a novel finding in vivo. Because **anecortave acetate** significantly inhibited pathologic retinal angiogenesis in this model, while not significantly affecting normal intraretinal vessels, it holds therapeutic potential for a number of human ocular conditions in which angiogenesis plays a critical pathologic role.
CT Medical Descriptors:
***retina neovascularization: DT, drug therapy**
***retrolental fibroplasia: DT, drug therapy**
angiogenesis
diabetic retinopathy: DT, drug therapy
retina macula degeneration: DT, drug therapy
drug mechanism
drug structure
nonhuman
rat
animal experiment
animal model
controlled study

animal tissue
article
priority journal
Drug Descriptors:
*steroid: AN, drug analysis
*steroid: DT, drug therapy
*steroid: PD, pharmacology
*steroid: VI, intravitreal drug administration
***anecortave: AN, drug analysis**
***anecortave: DT, drug therapy**
***anecortave: PD, pharmacology**
***anecortave: VI, intravitreal drug administration**
plasminogen activator inhibitor 1: EC, endogenous compound
unclassified drug
RN (**anecortave**) **7753-60-8**; (plasminogen activator inhibitor 1) 140208-23-7
CO Alcon (United States)

L59 ANSWER 5 OF 6 EMBASE
on STN
AN 2000082438 EMBASE
TI New therapies for the treatment of age-related **macular degeneration.**
AU Sarrafizadeh R.; Trese M.T.
CS M.T. Trese, Department of Biomedical Sciences, Eye Research Institute, Oakland University, Rochester, MI, United States. mgjt46@aol.com
SO Expert Opinion on Therapeutic Patents, (2000) 10/3 (333-341).
Refs: 62
ISSN: 1354-3776 CODEN: EOTPEG
CY United Kingdom
DT Journal; General Review
FS 012 Ophthalmology
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB Age-related **macular degeneration** (ARMD) is a leading cause of legal blindness in older adults. The visual loss caused by ARMD can be devastating and many of the current treatment modalities are ineffective or only of moderate benefit in preventing the progression of the disease. Furthermore, few treatment options are available to patients with more advanced cases of ARMD. This review highlights some aspects of our current understanding of ARMD and discusses recent patent applications related to the treatment of this disease. In particular, agents that promote retinal pigment epithelium (RPE) cell proliferation and compounds with anti-oxidant properties that may prove useful in the treatment of non-neovascular ARMD will be discussed. In addition, we review photodynamic therapy and anti-angiogenic compounds that show potential promise in the treatment of the neovascular form of ARMD.
CT Medical Descriptors:
*aging
***retina macula degeneration: DT, drug therapy**
***retina macula degeneration: TH, therapy**
blindness: DT, drug therapy
blindness: TH, therapy
cell proliferation
drug efficacy
patent
photodynamic therapy
pigment epithelium
visual impairment: DT, drug therapy
visual impairment: TH, therapy
human

nonhuman
clinical trial
review
Drug Descriptors:
acetylcarnitine: DT, drug therapy
alpha2a interferon: CT, clinical trial
alpha2a interferon: DT, drug therapy
anecortave: DV, drug development
angiogenesis inhibitor: DT, drug therapy
antioxidant: DT, drug therapy
antisense oligonucleotide
astaxanthin: DT, drug therapy
benzoporphyrin derivative: CT, clinical trial
benzoporphyrin derivative: DT, drug therapy
beta interferon: DT, drug therapy
beta interferon: PD, pharmacology
probucol: DT, drug therapy
steroid: DV, drug development
tranilast: DV, drug development
xanthophyll: CB, drug combination
xanthophyll: DT, drug therapy
zeaxanthin: CB, drug combination
zeaxanthin: DT, drug therapy
RN (acetylcarnitine) 14992-62-2; (alpha2a interferon) 76543-88-9; (**anecortave**) **7753-60-8**; (astaxanthin) 472-61-7; (benzoporphyrin derivative) 113719-89-4; (probucol) 23288-49-5; (tranilast) 53902-12-8; (xanthophyll) 127-40-2, 52842-48-5; (zeaxanthin) 144-68-3
CN (1) Verteporfin
CO (1) Ciba Geigy; Vyrex corporation; Howard foundation; Toray; Sigma Tau; Vogel; Pharmacyclics; Alcon; Kissei; Abbott

L59 ANSWER 6 OF 6 EMBASE
on STN
AN 1999404647 EMBASE
TI Changing therapeutic paradigms for exudative age-related **macular degeneration**: Antiangiogenic agents and photodynamic therapy.
AU Ciulla T.A.; Danis R.P.; Criswell M.; Pratt L.M.
CS T.A. Ciulla, IN Univ. Macular Degeneration Clinic, Department of Ophthalmology, Indiana University School Medicine, 702 Rotary Circle, Indianapolis, IN 46260, United States. tciulla@iupui.edu
SO Expert Opinion on Investigational Drugs, (1999) 8/12 (2173-2182).
Refs: 98
ISSN: 1354-3784 CODEN: EOIDER
CY United Kingdom
DT Journal; General Review
FS 012 Ophthalmology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB Age related **macular degeneration** (AMD) is the leading cause of irreversible visual loss in the United States. Overall, approximately 10-20% of patients with AMD exhibit the exudative form, which is responsible for most of the estimated 1.2 m cases of severe visual loss from AMD. Visual loss develops in the exudative form of AMD due to abnormal choroidal neovascular membranes (CNVM) that develop under the retina, leak serous fluid and blood, and ultimately cause a blinding disciform scar in, and under, the retina. Currently, the only well-studied and widely accepted method of treatment is laser photocoagulation of the CNVM. However, only a minority of patients with exudative AMD show well-demarcated 'classic' CNVM amenable to laser treatment, and at least

half of these patients suffer persistent or recurrent CNVM formation within two years. In addition, since the treatment itself causes a blinding central scotoma when the CNVM is located subfoveally, many clinicians do not treat subfoveal CNVM. With these treatment limitations, there has been a great deal of interest in alternative therapies for AMD, including anti-angiogenic agents and photodynamic therapy. Angiogenesis involves a complex interplay of cellular events involving a cascade of factors that are both inhibitory and stimulatory. Soluble growth factors have been the best-known cell modulating agents in ophthalmology, but there are a multitude of potential sites for inhibition of angiogenesis by pharmacological agents. With regard to photodynamic therapy, a photosensitising and low power laser light is used to activate the dye within the CNVM to cause vascular occlusion by a photochemical reaction. Closure of the CNVM is achieved without severe collateral damage to the non-vascular tissues as occurs with laser photocoagulation.

CT Medical Descriptors:
***retina macula age related degeneration: DT, drug therapy**
***retina macula age related degeneration: EP, epidemiology**
***retina macula age related degeneration: ET, etiology**
***retina macula age related degeneration: SU, surgery**
*photodynamic therapy
visual impairment: DT, drug therapy
visual impairment: EP, epidemiology
subretinal neovascularization: DT, drug therapy
subretinal neovascularization: EP, epidemiology
laser coagulation
central scotoma: CO, complication
pathogenesis
side effect: CO, complication
steroid therapy
drug clearance
human
oral drug administration
intravenous drug administration
topical drug administration
intravitreal drug administration
clinical trial
review
Drug Descriptors:
*angiogenesis inhibitor: CT, clinical trial
*angiogenesis inhibitor: DT, drug therapy
*angiogenesis inhibitor: PD, pharmacology
*photosensitizing agent: DV, drug development
*photosensitizing agent: DT, drug therapy
*photosensitizing agent: PR, pharmaceutics
*photosensitizing agent: PK, pharmacokinetics
*photosensitizing agent: PD, pharmacology
growth factor: EC, endogenous compound
antibody: DT, drug therapy
antibody: PD, pharmacology
vasculotropin: EC, endogenous compound
matrix metalloproteinase inhibitor: CT, clinical trial
matrix metalloproteinase inhibitor: DT, drug therapy
alpha interferon: AE, adverse drug reaction
alpha interferon: CT, clinical trial
alpha interferon: DT, drug therapy
alpha interferon: PD, pharmacology
prednisone: DT, drug therapy
steroid: DT, drug therapy
triamcinolone acetonide: CT, clinical trial
triamcinolone acetonide: DT, drug therapy
anecortave acetate: DV, drug development
thalidomide: CT, clinical trial

thalidomide: DV, drug development
thalidomide: DT, drug therapy
thalidomide: PD, pharmacology
phthalocyanine derivative: DV, drug development
rose bengal: DV, drug development
aspartylchlorin e6: DV, drug development
lutetium: CB, drug combination
lutetium: DV, drug development
etiopurpurin: DV, drug development
benzoporphyrin derivative: CT, clinical trial
benzoporphyrin derivative: DV, drug development
benzoporphyrin derivative: DT, drug therapy
benzoporphyrin derivative: PR, pharmaceutics
benzoporphyrin derivative: PK, pharmacokinetics
RN (vasculotropin) 127464-60-2; (prednisone) 53-03-2; (triamcinolone acetonide) 76-25-5; (thalidomide) 50-35-1; (rose bengal) 11121-48-5, 11139-83-6, 632-68-8; (aspartylchlorin e6) 110230-98-3; (lutetium) 7439-94-3; (benzoporphyrin derivative) 113719-89-4

=> => fil medline
FILE 'MEDLINE' ENTERED AT 16:31:53 ON 01 SEP 2004

FILE LAST UPDATED: 31 AUG 2004 (20040831/UP). FILE COVERS 1951 TO DATE.

On February 29, 2004, the 2004 MeSH terms were loaded. See HELP RLOAD for details. OLDMEDLINE now back to 1951.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2004 vocabulary. See http://www.nlm.nih.gov/mesh/ and http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a description of changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all l65

L65 ANSWER 1 OF 1 MEDLINE on STN
AN 2001087920 MEDLINE
DN PubMed ID: 11133880
TI The effect of an angiostatic steroid on neovascularization in a rat model of retinopathy of prematurity.
AU Penn J S; Rajaratnam V S; Collier R J; Clark A F
CS Department of Ophthalmology and Visual Sciences, Vanderbilt University School of Medicine, Nashville, Tennessee 37232-8808, USA.. john.penn@mcmail.vanderbilt.edu
NC EY07533 (NEI)
SO Investigative ophthalmology & visual science, **(2001 Jan)** 42 (1) 283-90.
Journal code: 7703701. ISSN: 0146-0404.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200101
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010118
AB PURPOSE: The inhibition of angiogenesis by angiostatic steroids has been demonstrated in a variety of systems, including rabbit and rat cornea. There is considerable interest in the therapeutic potential of this class of compounds for angiogenic ocular conditions such as diabetic

retinopathy, **macular degeneration**, and retinopathy of prematurity (ROP). This study was designed to test the capacity of an angiostatic steroid, **anecortave acetate**, to inhibit retinal neovascularization using a rat model of ROP and to investigate the mechanism of the effect. METHODS: At birth, rats were placed in an atmosphere of varying oxygen that produces retinal neovascular changes that approximate human ROP. The rats then received intravitreal injections of either **anecortave acetate** or vehicle at varying times, and all were subsequently placed in room air. Retinas were assessed for plasminogen activator inhibitor (PAI)-1 mRNA level by RNase protection assay at 1, 2, and 3 days after injection and for normal and abnormal blood vessel growth 3 days later. RESULTS: A significant reduction in the severity of abnormal retinal neovascularization was observed in the steroid-treated eyes compared with vehicle-injected eyes in ROP rats, yet the extent of normal total retinal vascular area was not significantly different. The drug had no effect on either retinal vascular area or neovascularization when tested in room air-raised control rats. Drug-injected eyes demonstrated a six- to ninefold increase in PAI-1 mRNA at 1 to 3 days after injection. CONCLUSIONS: This study represents the first therapeutic effect of an angiostatic steroid in an animal model of neovascular retinopathy. Additionally, the induction of PAI-1 indicates a mechanism of action for this class of compounds, and this is a novel finding in vivo. Because **anecortave acetate** significantly inhibited pathologic retinal angiogenesis in this model, while not significantly affecting normal intraretinal vessels, it holds therapeutic potential for a number of human ocular conditions in which angiogenesis plays a critical pathologic role.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*Angiogenesis Inhibitors: TU, therapeutic use
Animals
Animals, Newborn
Blotting, Northern
Disease Models, Animal
Infant, Newborn
Injections
Nuclease Protection Assays
Plasminogen Activator Inhibitor 1: BI, biosynthesis
Plasminogen Activator Inhibitor 1: GE, genetics
*Pregnadienediols: TU, therapeutic use
RNA Probes
RNA, Messenger: BI, biosynthesis
Random Allocation
Rats
Rats, Sprague-Dawley
Retinal Neovascularization: ME, metabolism
Retinal Neovascularization: PA, pathology
*Retinal Neovascularization: PC, prevention & control
*Retinopathy of Prematurity: DT, drug therapy
Retinopathy of Prematurity: ME, metabolism
Retinopathy of Prematurity: PA, pathology
Vitreous Body

CN 0 (Angiogenesis Inhibitors); 0 (Plasminogen Activator Inhibitor 1); 0 (Pregnadienediols); 0 (RNA Probes); 0 (RNA, Messenger); 0 (**anecortave acetate**)

=> => fil biosis
FILE 'BIOSIS' ENTERED AT 16:34:26 ON 01 SEP 2004

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT

FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 26 August 2004 (20040826/ED)

FILE RELOADED: 19 October 2003.

=> d l68 all tot

L68 ANSWER 1 OF 8 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2003:219511 BIOSIS
DN PREV200300219511
TI **Anecortave acetate.** Treatment of age-related **macular degeneration**, angiogenesis inhibitor.
AU Sorbera, L. A. [Reprint Author]; Leeson, P. A. [Reprint Author]; Castaner, J. [Reprint Author]; Bayes, M. [Reprint Author]
CS Prous Science, 08080, P.O. Box 540, Barcelona, Spain
SO Drugs of the Future, (November 2002) Vol. 27, No. 11, pp. 1039-1048. print.
ISSN: 0377-8282.
DT Article
LA English
ED Entered STN: 7 May 2003
Last Updated on STN: 7 May 2003
CC Cytology - Animal 02506
Cytology - Human 02508
Pathology - Therapy 12512
Cardiovascular system - Physiology and biochemistry 14504
Sense organs - Pathology 20006
Nervous system - Pathology 20506
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Pharmacology - Cardiovascular system 22010
Pharmacology - Sense organs, associated structures and functions 22031
IT Major Concepts
Methods and Techniques; Pharmacology
IT Parts, Structures, & Systems of Organisms
microvascular endothelial cell: circulatory system; umbilical vein endothelial cell: circulatory system
IT Diseases
age-related **macular degeneration**: eye disease, drug therapy
Macular Degeneration (MeSH)
IT Diseases
blindness: eye disease, nervous system disease
Blindness (MeSH)
IT Chemicals & Biochemicals
anecortave acetate: cardiovascular-drug, ophthalmic-drug, synthesis
IT Methods & Equipment
chemical synthesis: laboratory techniques; condensation: laboratory techniques
IT Miscellaneous Descriptors
angiogenesis: inhibition
ORGN Classifier
Galliformes 85536
Super Taxa
Aves; Vertebrata; Chordata; Animalia
Organism Name
chicken (common)
Taxa Notes
Animals, Birds, Chordates, Nonhuman Vertebrates, Vertebrates
ORGN Classifier
Hominidae 86215

Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
U937 cell line (cell line)
human (common)
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
ORGN Classifier
Leporidae 86040
Super Taxa
Lagomorpha; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
rabbit (common)
Taxa Notes
Animals, Chordates, Lagomorphs, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Vertebrates
ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
rat (common)
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates
RN **7753-60-8 (anecortave acetate)**

L68 ANSWER 2 OF 8 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2003:175226 BIOSIS
DN PREV200300175226
TI Motion Ophthalmoscopy Macula (MOM).
AU Ciardella, A. P. [Reprint Author]; Hathiromani, S. [Reprint Author]; Orlock, D. [Reprint Author]; Borodoker, N. [Reprint Author]; Yannuzzi, L. A. [Reprint Author]
CS Ophthalmology, Manhattan Eye, Ear and Throat Hospital, New York, NY, USA
SO ARVO Annual Meeting Abstract Search and Program Planner, (2002) Vol. 2002, pp. Abstract No. 4340. cd-rom.
Meeting Info.: Annual Meeting of the Association For Research in Vision and Ophthalmology. Fort Lauderdale, Florida, USA. May 05-10, 2002.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 9 Apr 2003
Last Updated on STN: 9 Apr 2003
AB Purpose: To describe a new technique for imaging pathologic changes over time in the fundus: Motion Opthalmoscopy of the **Macula** (MOM). Clinical examples utilizing the fusion of separate digital images into a sequential, clinical course will be presented. Methods: Commerciaally available software was used to fuse in a movie sequential digital fundus photographs. Results: Three movies demonstrating the clinical course of three patients with **macular** disease. The first movie shows spontaneous resolution of a submacular hemorrhage in a patient with polypoidal choroidal vasculopathy, over 1-year follow-up. The second movie illustrates the resolution of a serous-sanguineos neurosensory **macular** detachment in a patient with idiopathic perifoveal telangectasia, after treatment with a single intravitreal injection of **anecortave acetate.** The follow-up was 1 year. The third movie shows the clinical course of a patient with retinal angiomatous proliferation, a variant of age related **macular degeneration**, over 1-year period. Conclusion: MOM is a simple but innovative way of showing the clinical course of a patient over time. It is ideal for a web site presentation, as well as interactive presentation to a group at meetings. It is also a very effective mean of education for

the patient itself.
CC General biology - Symposia, transactions and proceedings 00520
Pathology - Therapy 12512
Sense organs - Physiology and biochemistry 20004
Sense organs - Pathology 20006
Nervous system - Pathology 20506
Pharmacology - Clinical pharmacology 22005
Pharmacology - Sense organs, associated structures and functions 22031
IT Major Concepts
Methods and Techniques; Ophthalmology (Human Medicine, Medical Sciences)
IT Parts, Structures, & Systems of Organisms
fundus: sensory system
IT Diseases
age related **macular degeneration**: eye disease
Macular Degeneration (MeSH)
IT Diseases
idiopathic perifoveal telangectasia: eye disease
IT Diseases
macular disease: eye disease
IT Diseases
polypoidal choroidal vasculopathy: eye disease
IT Diseases
retinal angiomatous proliferation: eye disease
IT Diseases
serous-sanguineos neurosensory macular detachment: eye disease, nervous system disease
IT Diseases
submacular hemorrhage: eye disease
IT Chemicals & Biochemicals
anecortave acetate: ophthalmic-drug, intravitreal administration
IT Methods & Equipment
motion ophthalmoscopy of the macula: clinical techniques, diagnostic techniques; sequential digital fundus photography: clinical techniques, diagnostic techniques
IT Miscellaneous Descriptors
clinical course; digital images; interactive presentation; pathologic changes; web site presentation
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human (common): patient
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN **7753-60-8 (anecortave acetate)**

L68 ANSWER 3 OF 8 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2003:154979 BIOSIS
DN PREV200300154979
TI Sub-Tenon's Administration of the Angiostatic Agent **Anecortave Acetate** in AMD Patients with Subfoveal Choroidal Neovascularization (CNV) - the Clinical Outcome.
AU Slakter, J. S. [Reprint Author]; Singerman, L. J.; Yannuzzi, L. A.; Russell, S. R.; Hudson, H. L.; Jerdan, J.; Zilliox, P.; Robertson, S.; Anecortave Acetate Study Group
CS Vitreous Ret Mac Consult of NY, New York, NY, USA
SO ARVO Annual Meeting Abstract Search and Program Planner, (2002) Vol. 2002, pp. Abstract No. 2909. cd-rom.
Meeting Info.: Annual Meeting of the Association For Research in Vision and Ophthalmology. Fort Lauderdale, Florida, USA. May 05-10, 2002.

DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 26 Mar 2003
Last Updated on STN: 26 Mar 2003
AB Purpose: To evaluate efficacy and safety of the angiostatic agent **anecortave acetate** for inhibition of subfoveal CNV lesion growth in AMD patients in two clinical studies. Changes in visual acuity and lesion characteristic are being evaluated as measures of efficacy. Methods: In both studies, a sterile suspension of **anecortave acetate** or placebo is administered as a sub-Tenon's retrobulbar injection via a specially designed cannula. The first study is a masked randomized evaluation of three **anecortave acetate** dosages versus placebo, with optional re-injection at 6-month intervals. The second masked randomized study evaluates **anecortave acetate** or placebo following initial Visudyne PDT. In this 6-month study, patients are randomized to a single injection of one of two dosages of **anecortave acetate** or to placebo. Patients with either predominantly classic or minimally classic subfoveal lesions are eligible for this study, which is evaluating the effect of **anecortave acetate** on visual acuity and post-PDT lesion changes. Results: Enrollment is complete in both studies with a total of 264 patients enrolled by 22 clinical sites in North America and the EU. In the first study, 128 patients have been enrolled and treated, with 78 of these patients receiving at least one additional injection. In the second study, 115 of the 136 enrolled and treated patients have completed the study and been exited. In both of these studies, digital fluorescein and indocyanine green angiograms are being evaluated by the Digital Angiography Reading Center (DARC), and lesion characteristics (lesion area, CNV area, classic CNV area) will be compared over time across treatment groups. Conclusion: Differences across treatment groups in both best-corrected logMAR visual acuity and angiographic lesion characteristics will be compared and discussed.
CC General biology - Symposia, transactions and proceedings 00520
Pathology - Therapy 12512
Sense organs - Pathology 20006
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Pharmacology - Sense organs, associated structures and functions 22031
IT Major Concepts
Ophthalmology (Human Medicine, Medical Sciences); Pharmacology
IT Diseases
AMD: eye disease, age-related **macular degeneration**
Macular Degeneration (MeSH)
IT Diseases
subfoveal choroidal neovascularization: eye disease
Choroidal Neovascularization (MeSH)
IT Chemicals & Biochemicals
Visudyne: photosensitizer drug; **anecortave acetate**: ophthalmic-drug, angiostatic agent, efficacy, safety, sub-Tenon's retrobulbar injection
IT Methods & Equipment
digital fluorescein angiography: clinical techniques, diagnostic techniques; indocyanine green angiography: clinical techniques, diagnostic techniques; photodynamic therapy: clinical techniques, therapeutic and prophylactic techniques
IT Miscellaneous Descriptors
clinical outcome; visual acuity
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name

human (common): patient
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN 129497-78-5 (Visudyne)
7753-60-8 (anecortave acetate)

L68 ANSWER 4 OF 8 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2003:142495 BIOSIS
DN PREV200300142495
TI **Anecortave Acetate** Administered Sub-Tenon's Retrobulbar with and without Visudyne PDT in Patients with Subfoveal Age-Related **Macular Degeneration** (AMD) - Clinical Safety Profile.
AU D'Amico, D. J. [Reprint Author]; Duker, J.; Regillo, C.; Schneebaum, C.; Beasley, C.
CS Harvard Medical School, MA Eye and Ear Infirmary, Boston, MA, USA
SO ARVO Annual Meeting Abstract Search and Program Planner, (2002) Vol. 2002, pp. Abstract No. 569. cd-rom.
Meeting Info.: Annual Meeting of the Association For Research in Vision and Ophthalmology. Fort Lauderdale, Florida, USA. May 05-10, 2002.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 19 Mar 2003
Last Updated on STN: 19 Mar 2003
AB Purpose: Since 1998, the Independent Safety Committee has provided an independent medical expert review of safety information related to the two ongoing clinical trials evaluating the angiostatic agent **anecortave acetate** when administered as a sub-Tenon's retrobulbar bolus to patients with subfoveal AMD. This Committee is composed of three clinical retina specialists in addition to an internist and the Alcon Medical Monitor responsible for the safety oversight of these studies. Meetings of the Committee have included both telephone conferences and in-person meetings to periodically review the accumulating body of safety information. Methods: Safety information is derived from general physical examinations and dilated ophthalmic examinations of the patients in both trials including indocyanine green and/or fluorescein angiograms. Results: Enrollment has been completed for both of these studies. In study C-98-03, which evaluates **anecortave acetate** monotherapy, 128 patients have been enrolled and treated. In study C-00-07, which evaluates the effect of **anecortave acetate** following PDT treatment with Visudyne(TM), 136 patients have been enrolled and treated. During the most recent Safety Committee meeting, 400 safety events from C-98-03 and 180 safety events from C-00-07 were reviewed and discussed. Based on their review of safety changes, there has been no request by the Committee to make any study design changes or to interrupt enrollment in either study. Conclusion: The Independent Safety Committee has reviewed the accumulating safety reports of all changes in patients enrolled in two clinical trials evaluating the effect of **anecortave acetate** on patients with subfoveal AMD. There have been no clinically significant safety issues identified by the Independent Safety Committee to date.
CC General biology - Symposia, transactions and proceedings 00520
Radiation biology - Radiation and isotope techniques 06504
Pathology - Therapy 12512
Cardiovascular system - Heart pathology 14506
Cardiovascular system - Blood vessel pathology 14508
Sense organs - Pathology 20006
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Pharmacology - Cardiovascular system 22010
Pharmacology - Sense organs, associated structures and functions 22031
IT Major Concepts

Cardiovascular Medicine (Human Medicine, Medical Sciences); Ophthalmology (Human Medicine, Medical Sciences); Pharmacology; Radiology (Medical Sciences)
IT Diseases
subfoveal age-related **macular degeneration**: eye disease, vascular disease, drug therapy, radiotherapy
IT Chemicals & Biochemicals
anecortave acetate: cardiovascular-drug, ophthalmic-drug, angiostatic activity, safety, sub-tenon's retrobulbar bolus; visudyne: ophthalmic-drug, radiosensitizer-drug
IT Methods & Equipment
PDT [photodynamic therapy]: clinical techniques, therapeutic and prophylactic techniques; fluorescein angiogram: clinical techniques, diagnostic techniques, imaging and microscopy techniques, laboratory techniques, spectrum analysis techniques; indocyanine green angiogram: clinical techniques, diagnostic techniques, imaging and microscopy techniques, laboratory techniques
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human (common): patient
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN **7753-60-8** (**anecortave acetate**)
129497-78-5 (visudyne)

L68 ANSWER 5 OF 8 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2001:319945 BIOSIS
DN PREV200100319945
TI Sub-Tenon's retrobulbar **anecortave acetate** with and without Visudyne PDT in patients with subfoveal age-related **macular degeneration** (AMD): A review of the emerging clinical safety profile of this new experimental treatment.
AU D'Amico, D. J. [Reprint author]; Adamis, A. P. [Reprint author]; Duker, J.; Regillo, C.; Schneebaum, C.; Beasley, C.
CS Harvard Medical School, MA Eye and Ear Infirmary, Boston, MA, USA
SO IOVS, (March 15, 2001) Vol. 42, No. 4, pp. S232. print.
Meeting Info.: Annual Meeting of the Association for Research in Vision and Ophthalmology. Fort Lauderdale, Florida, USA. April 29-May 04, 2001.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 4 Jul 2001
Last Updated on STN: 19 Feb 2002
CC Pathology - Diagnostic 12504
General biology - Symposia, transactions and proceedings 00520
Biochemistry studies - General 10060
Pathology - Therapy 12512
Cardiovascular system - Blood vessel pathology 14508
Integumentary system - Pathology 18506
Sense organs - Physiology and biochemistry 20004
Sense organs - Pathology 20006
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Pharmacology - Sense organs, associated structures and functions 22031
Toxicology - General and methods 22501
Toxicology - Pharmacology 22504
IT Major Concepts
Ophthalmology (Human Medicine, Medical Sciences); Methods and Techniques; Pharmacology
IT Parts, Structures, & Systems of Organisms

conjunctiva: sensory system; eye: sensory system; fovea: sensory system; lens: sensory system; macula: sensory system; retina: sensory system

IT Diseases
abnormal vision: eye disease, toxicity

IT Diseases
cataract: eye disease, toxicity
Cataract (MeSH)

IT Diseases
decreased visual acuity: eye disease, toxicity

IT Diseases
eye pain: eye disease, toxicity

IT Diseases
ocular foreign body sensation: eye disease, toxicity, side effect

IT Diseases
ocular hyperemia: eye disease, toxicity, side effect

IT Diseases
ocular pruritus: eye disease, integumentary system disease, toxicity

IT Diseases
ptosis: eye disease, toxicity

IT Diseases
retinal hemorrhage: eye disease, toxicity, vascular disease
Retinal Hemorrhage (MeSH)

IT Diseases
subconjunctival hemorrhage: eye disease, toxicity, vascular disease
Eye Hemorrhage (MeSH)

IT Diseases
subfoveal age-related **macular degeneration**: eye disease, treatment

IT Diseases
tearing: eye disease, toxicity

IT Chemicals & Biochemicals
Visudyne: ophthalmic-drug, side effects, toxicity; **anecortave acetate**: ophthalmic-drug, clinical trial, efficacy, safety, sub-Tenon's retrobulbar administration, toxicity; fluorescein: diagnostic agent; indocyanine green: diagnostic agent

IT Methods & Equipment
PDT [photodynamic therapy]: therapeutic method; fluorescein angiography: diagnostic method; indocyanine green angiography: diagnostic method

IT Miscellaneous Descriptors
visual acuity; Meeting Abstract

ORGN Classifier
Hominidae 86215

Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia

Organism Name
human: patient

Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

RN 129497-78-5 (Visudyne)
7753-60-8 (anecortave acetate)
2321-07-5 (fluorescein)
3599-32-4 (indocyanine green)

L68 ANSWER 6 OF 8 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2001:319941 BIOSIS
DN PREV200100319941
TI Sub-Tenon's retrobulbar **anecortave acetate** with and without VisudyneTM photodynamic therapy (PDT) in patients with subfoveal choroidal neovascularization (CNV) in age-related **macular degeneration** (AMD).
AU Singerman, L. J. [Reprint author]; Yannuzzi, L. A.; Russell, S.; Hudson,

H. L.; Jerdan, J.; Anecortave Acetate Study Group
CS Retina Associates of Cleveland, Cleveland, OH, USA
SO IOVS, (March 15, 2001) Vol. 42, No. 4, pp. S231. print.
Meeting Info.: Annual Meeting of the Association for Research in Vision and Ophthalmology. Fort Lauderdale, Florida, USA. April 29-May 04, 2001.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 4 Jul 2001
Last Updated on STN: 19 Feb 2002
CC Cardiovascular system - Heart pathology 14506
General biology - Symposia, transactions and proceedings 00520
Pathology - Therapy 12512
Cardiovascular system - Blood vessel pathology 14508
Sense organs - Physiology and biochemistry 20004
Sense organs - Pathology 20006
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Pharmacology - Sense organs, associated structures and functions 22031
IT Major Concepts
Cardiovascular Medicine (Human Medicine, Medical Sciences); Ophthalmology (Human Medicine, Medical Sciences); Methods and Techniques; Pharmacology
IT Parts, Structures, & Systems of Organisms
choroid: sensory system; fovea: sensory system; macula: sensory system
IT Diseases
age-related **macular degeneration**: eye disease, treatment
Macular Degeneration (MeSH)
IT Diseases
subfoveal choroidal neovascularization: eye disease, vascular disease, treatment
Choroidal Neovascularization (MeSH)
IT Chemicals & Biochemicals
Visudyne: ophthalmic-drug; **anecortave acetate**: ophthalmic-drug, dosage, efficacy, sub-Tenon's retrobulbar administration
IT Methods & Equipment
photodynamic therapy: therapeutic method
IT Miscellaneous Descriptors
visual acuity; Meeting Abstract
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human: patient
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN 129497-78-5 (Visudyne)
7753-60-8 (anecortave acetate)

L68 ANSWER 7 OF 8 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2001:317760 BIOSIS
DN PREV200100317760
TI Subtenons retrobulbar **anecortave acetate** with and without Visudyne PDT in patients with subfoveal age-related **macular degeneration** (AMD): A Digital Angiography Reading Center (DARC) review of baseline lesion characteristics.
AU Slakter, J. S. [Reprint author]; Freund, K. B. [Reprint author]; Coleman, H. [Reprint author]; Wheatley, M. [Reprint author]; Carvalho, C. [Reprint author]; Negrao, S. [Reprint author]; Zilliox, P.
CS DARC, New York, NY, USA

SO IOVS, (March 15, 2001) Vol. 42, No. 4, pp. S231. print.
Meeting Info.: Annual Meeting of the Association for Research in Vision and Ophthalmology. Fort Lauderdale, Florida, USA. April 29-May 04, 2001.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 4 Jul 2001
Last Updated on STN: 19 Feb 2002
CC Blood - Blood and lymph studies 15002
General biology - Symposia, transactions and proceedings 00520
Biochemistry studies - General 10060
Biochemistry studies - Lipids 10066
Pathology - Diagnostic 12504
Pathology - Therapy 12512
Blood - Blood cell studies 15004
Sense organs - Physiology and biochemistry 20004
Sense organs - Pathology 20006
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Pharmacology - Sense organs, associated structures and functions 22031
Toxicology - General and methods 22501
Toxicology - Pharmacology 22504
IT Major Concepts
Ophthalmology (Human Medicine, Medical Sciences); Methods and Techniques; Pharmacology
IT Parts, Structures, & Systems of Organisms
blood: blood and lymphatics; fovea: sensory system; fundus: sensory system; macula: sensory system
IT Diseases
subfoveal age-related **macular degeneration**: eye disease, characterization, treatment
IT Chemicals & Biochemicals
Visudyne: ophthalmic-drug; **anecortave acetate**: ophthalmic-drug, clinical trial, efficacy, subtenon retrobulbar administration, toxicity; fluorescein: diagnostic agent; indocyanine green: diagnostic agent; lipid
IT Methods & Equipment
PDT [photodynamic therapy]: therapeutic method; fluorescein angiography: diagnostic method; indocyanine green angiography: diagnostic method
IT Miscellaneous Descriptors
Meeting Abstract; Digital Angiography Reading Center: company/organization
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human: patient
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN 129497-78-5 (Visudyne)
7753-60-8 (anecortave acetate)
2321-07-5 (fluorescein)
3599-32-4 (indocyanine green)

L68 ANSWER 8 OF 8 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2001:78076 BIOSIS
DN PREV200100078076
TI The effect of an angiostatic steroid on neovascularization in a rat model of retinopathy of prematurity.
AU Penn, John S. [Reprint author]; Rajaratnam, Veeraramani S.; Collier, Robert J.; Clark, Abbot F.

CS Department of Ophthalmology and Visual Sciences, Vanderbilt University School of Medicine, 2115 21st Avenue South, 8016 Medical Center East, Nashville, TN, 37232-8808, USA
john.penn@mcmail.vanderbilt.edu
SO IOVS, (January, 2001) Vol. 42, No. 1, pp. 283-290. print.
DT Article
LA English
ED Entered STN: 7 Feb 2001
Last Updated on STN: 12 Feb 2002
AB Purpose. The inhibition of angiogenesis by angiostatic steroids has been demonstrated in a variety of systems, including rabbit and rat cornea. There is considerable interest in the therapeutic potential of this class of compounds for angiogenic ocular conditions such as diabetic retinopathy, **macular degeneration**, and retinopathy of prematurity (ROP). This study was designed to test the capacity of an angiostatic steroid, **anecortave acetate**, to inhibit retinal neovascularization using a rat model of ROP and to investigate the mechanism of the effect. Methods. At birth, rats were placed in an atmosphere of varying oxygen that produces retinal neovascular changes that approximate human ROP. The rats then received intravitreal injections of either **anecortave acetate** or vehicle at varying times, and all were subsequently placed in room air. Retinas were assessed for plasminogen activator inhibitor (PAI)-1 mRNA level by RNase protection assay at 1, 2, and 3 days after injection and for normal and abnormal blood vessel growth 3 days later. Results. A significant reduction in the severity of abnormal retinal neovascularization was observed in the steroid-treated eyes compared with vehicle-injected eyes in ROP rats, yet the extent of normal total retinal vascular area was not significantly different. The drug had no effect on either retinal vascular area or neovascularization when tested in room air-raised control rats. Drug-injected eyes demonstrated a six- to ninefold increase in PAI-1 mRNA at 1 to 3 days after injection. Conclusions. This study represents the first therapeutic effect of an angiostatic steroid in an animal model of neovascular retinopathy. Additionally, the induction of PAI-1 indicates a mechanism of action for this class of compounds, and this is a novel finding in vivo. Because **anecortave acetate** significantly inhibited pathologic retinal angiogenesis in this model, while not significantly affecting normal intraretinal vessels, it holds therapeutic potential for a number of human ocular conditions in which angiogenesis plays a critical pathologic role.
CC Pharmacology - Sense organs, associated structures and functions 22031
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Pathology - Therapy 12512
Sense organs - Physiology and biochemistry 20004
Sense organs - Pathology 20006
Pharmacology - General 22002
IT Major Concepts
Pharmacology; Sense Organs (Sensory Reception)
IT Parts, Structures, & Systems of Organisms
retina: sensory system
IT Diseases
retinopathy of prematurity: eye disease, treatment
Retinopathy of Prematurity (MeSH)
IT Chemicals & Biochemicals
anecortave acetate [4,9(11)-pregnadien-17-alpha,21-diol-3,20-dione-21-acetate]: ophthalmic-drug, angiostatic steroid, structure, usefulness; plasminogen activator inhibitor-1 messenger RNA: induction
IT Methods & Equipment
RNase protection assay: analytical method
IT Miscellaneous Descriptors
retinal neovascularization: inhibition
ORGN Classifier

Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
rat: animal model, strain-Sprague-Dawley
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates
RN **7753-60-8 (anecortave acetate)**
7753-60-8 (4,9(11)-pregnadien-17-alpha,21-diol-3,20-dione-21-acetate)

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L75 ANSWER 1 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2004-315778 [29] WPIX
DNC C2004-119770
TI Treatment, prevention and inhibition of angiogenesis-mediated diseases or conditions of retina or choroid comprises administration of a composition comprising an immunophilin binding active agent e.g. rapamycin.
DC B05
IN LATIES, A; LOU, Z; WEN, R
PA (UYPE-N) UNIV PENNSYLVANIA
CYC 105
PI WO 2004027027 A2 20040401 (200429)* EN 27 C12N000-00
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW
ADT WO 2004027027 A2 WO 2003-US29188 20030918
PRAI US 2002-412088P 20020918
IC ICM C12N000-00

AB WO2004027027 A UPAB: 20040505
NOVELTY - Treatment, prevention and inhibition of angiogenesis-mediated diseases or conditions of the retina or choroid in a mammal comprises the administration of a composition (I) comprising an immunophilin binding active agent.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a composition comprising rapamycin, a rapamycin analog or tacrolimus and a carrier suitable for administration to the eye or eye tissue.
ACTIVITY - Antiangiogenic; Antidiabetic; Ophthalmological; Vasotropic.
The inhibition of choroidal neovasculature by rapamycin was tested in Sprague-Dawley rats. The results showed that rapamycin demonstrated a remarkable ability to inhibit new blood vessel formation.
MECHANISM OF ACTION - None given.
USE - (I) is useful for the treatment, prevention and inhibition of angiogenesis-mediated diseases or conditions (diabetic retinopathy, **macular degeneration** or preferably choroidal neovascularization (occurs in retinal or subretinal disorders of age-related **macular degeneration**, presumed ocular histoplasmosis syndrome, myopic **degeneration**, angioid streaks or ocular trauma) or (exudative) age-related **macular degeneration**) of the retina or choroid in a mammal. (I) is also useful in improving the ocular vision in retinal disorders characterized by choroidal neovascularization or angiogenesis of the retina of eye of the mammal (all claimed).
Dwg.0/3
FS CPI
FA AB; DCN
MC CPI: B01-A02; B01-B02; B01-C06; B01-D02; B02-R; B02-T; B03-A; B04-A06; B04-B03C; B04-C01; B04-H05; B04-N04; B05-A03B; B05-C06; B06-A01; B06-D01; B06-D03; B06-D18; B06-E05; B07-A01; B07-A03; B07-D03; B07-D04C; B07-D10; B07-F01; B10-A09B; B10-A12A; B10-B01B; B10-B02A; B14-D05C; B14-D06; B14-F02F2; B14-J02B1; B14-L01; B14-L06; B14-N03; B14-S04
TECH UPTX: 20040505
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: (I) is preferably rapamycin, its analog or tacrolimus. (I) is also administered with another agent (II) for the treatment of angiogenesis or neovascularization (particularly choroidal neovasculature (CNV)). (II) is preferably pyrrolidine, dithiocarbamate (nuclear factor kappa B kinase inhibitor), squalamine, TPN 470 analogue and fumagillin, protein kinase C inhibitors, Tie(tyrosine kinase inhibitor)-1 and Tie-2 kinase inhibitors, inhibitors of vascular endothelial growth factor (VEGF) receptor kinase, proteosome inhibitors such as Velcade (bortezomin), bortezomib, for injection, ranibuzumab (Lucentis(ranibizumab) and other antibodies directed to the same target, pegaptanib (Macugen (pegaptanin sodium), vitronectin receptor antagonists, such as cyclic peptide antagonists of vitronectin receptor-type integrins, a-(vaso active intestinal peptide)VIP-3 integrin antagonists, a-VIP-1 integrin antagonists, thiazolidinediones such as rosiglitazone or troglitazone, interferon, including y-interferon or interferon targeted to CNV by use of dextran and metal coordination, pigment epithelium derived factor, endostatin, angiostatin, **anecortave acetate**, acetonide, triamcinolone, tetrathiomolybdate, Accutane (isotretinoine) (13-cis retinoic acid), ACE inhibitors such as quinopril or perindonil, inhibitors of mammalian target of rapamycin, 3-aminothalidomide, pentoxifylline, 2-methoxyestradiol, colchicines, AGM-1470, cyclooxygenase inhibitors such as nepafenac, rofecoxib, and diclofenac, t-RNA synthase modulator, metalloprotease 13 inhibitor, acetylcholinesterase inhibitor, potassium channel blockers, endorepellin, arginine deiminase, epigallocatechin-3-gallate, cerivastatin, analogues of suramin, and Visudyne.
ABEX UPTX: 20040505
ADMINISTRATION - Administration of (I) is intraocular, subretinal,

subscleral, intrachoroidal, subconjunctival, topical, oral or parenteral (claimed), at a dosage of 0.1-300 (preferably 1-10) mg/kg/day.

L75 ANSWER 2 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2004-203578 [19] WPIX
DNC C2004-080256
TI Use of **anecortave acetate** to maintain or prevent the loss of visual acuity and inhibit lesion growth associated with age related **macular degeneration.**
DC B01
IN JERDAN, J A; ROBERTSON, S M; ZILLIOX, P
PA (JERD-I) JERDAN J A; (ROBE-I) ROBERTSON S M; (ZILL-I) ZILLIOX P; (ALCO-N) ALCON INC
CYC 38
PI WO 2004012742 A1 20040212 (200419)* EN 29 A61K031-56
RW: AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PT RO SE SI SK TR
W: AU BR CA CN JP KR MX PH PL RU US ZA
US 2004127472 A1 20040701 (200444) A61K031-56
AU 2003281817 A1 20040223 (200453) A61K031-56
ADT WO 2004012742 A1 WO 2003-US20154 20030626; US 2004127472 A1 Provisional US 2002-401220P 20020805, US 2003-606501 20030626; AU 2003281817 A1 AU 2003-281817 20030626
FDT AU 2003281817 A1 Based on WO 2004012742
PRAI US 2002-401220P 20020805; US 2003-606501 20030626
IC ICM A61K031-56
AB WO2004012742 A UPAB: 20040525
NOVELTY - Prevention of the loss of visual acuity, maintenance of visual acuity and inhibition of lesion growth associated with age related **macular degeneration** comprises juxtascleral administration of **anecortave acetate** (I) or its alcohol.
ACTIVITY - Ophthalmological.
MECHANISM OF ACTION - Protease inhibitor; Angiogenesis inhibitor; Urokinase-like plasminogen activator inhibitor; matrix metalloproteinase-3 inhibitor.
USE - (I) is useful for the preparation of a medicament for maintaining visual acuity, prevention of the loss of visual acuity and for the inhibition of lesion growth associated with age related **macular degeneration** (claimed).
(I) was analysed for severe vision loss at 6 month by comparing with baseline among treatment groups. The result showed that at 15 mg, (I) was 96.97% of less than 6 lines worse when compared to placebo treatment 76.67%.
ADVANTAGE - (I) is safe and does not produce glucocorticoid receptor-mediated steroidal side effects.
Dwg.0/5
FS CPI
FA AB; DCN
MC CPI: B01-C03; B01-C05; B14-C03
ABEX UPTX: 20040525
ADMINISTRATION - Administration of (I) is 3-30 (preferably 15) mg as a juxtascleral depot or juxtascleral implant (claimed).

L75 ANSWER 3 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-672690 [72] WPIX
CR 2001-425112 [45]; 2001-432457 [46]; 2004-051015 [05]
DNN N2002-531711 DNC C2002-189451
TI Ophthalmic drug delivery device for clinical studies, incl
comprising 4,9 (11)-pregnadien-17alpha,21-diol-3,20-dione
4,9(11)-pregnadien-17alpha,21-diol-3,20-dione-21-acetate.
DC B01 B07 P32
IN YAACOBI, Y

This is your compound - see pages 82-84

PA (ALCO-N) ALCON UNIVERSAL LTD
CYC 1
PI US 6413540 B1 20020702 (200272)* 13 A61F002-00
ADT US 6413540 B1 Provisional US 1999-160673P 19991021, US 2000-660000 20000912
PRAI US 1999-160673P 19991021; US 2000-660000 20000912
IC ICM A61F002-00
AB US 6413540 B UPAB: 20040120
NOVELTY - Ophthalmic drug delivery device comprises a body having a scleral surface for placement proximate a sclera and a well having an opening to the scleral surface, and an inner core in the well. The inner core comprises 4,9 (11)-pregnadien-17 alpha ,21-diol-3,20-dione, 4,9(11)-pregnadien-17 alpha ,21-diol-3,20-dione-21-acetate or eliprodil.
USE - Used in clinical studies for localized delivery of active agent to the human eye having era, choroid and retina, Tenon's capsule and **macula.** In ophthalmic drug delivery, the device is especially useful for localized delivery of pharmaceutically active agents to the posterior segment of a eye to combat age related **macular degeneration** and choroidal neovascularization, retinopathies, retinitis, uveitis, **macular** edema and glaucoma.
ADVANTAGE - The device is safe, effective, rate-controlled, and suitable for localized delivery of active agents to any body tissue. The surgical procedure for implanting the device is safe, simple, quick and capable of being performed in an outpatient setting. The device is easy and economical to manufacture.
Dwg.0/7
FS CPI GMPI
FA AB; DCN
MC CPI: B01-C06; B07-D05; B14-N03
TECH UPTX: 20021108
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Device: The body comprises a biocompatible, non-bioerodable material. The inner core is a tablet, comprising a hydrogel. The active agent is positioned within the hydrogel.

L75 ANSWER 4 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-451774 [48] WPIX
DNN N2001-334447 DNC C2001-136453
TI Plaque for intravitreal administration for treating intraoccular conditions such as retinopathies, comprises inner and outer surfaces, and one or more guide units for guiding needle into interior portion of eye.
DC B07 P32
IN BILLSON, F A; GILLIES, M C; PENFOLD, P L
PA (UNSY) UNIV SYDNEY; (BILL-I) BILLSON F A; (GILL-I) GILLIES M C; (PENF-I) PENFOLD P L
CYC 95
PI WO 2001049226 A1 20010712 (200148)* EN 20 A61F009-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001026527 A 20010716 (200169) A61F009-00
EP 1253892 A1 20021106 (200281) EN A61F009-00
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
US 2003060763 A1 20030327 (200325) A61M005-00
JP 2003518987 W 20030617 (200349) 22 A61F009-007
ADT WO 2001049226 A1 WO 2001-AU12 20010108; AU 2001026527 A AU 2001-26527 20010108; EP 1253892 A1 EP 2001-901015 20010108, WO 2001-AU12 20010108; US 2003060763 A1 WO 2001-AU12 20010108, US 2002-169230 20020912; JP 2003518987 W JP 2001-549595 20010108, WO 2001-AU12 20010108
FDT AU 2001026527 A Based on WO 2001049226; EP 1253892 A1 Based on WO

2001049226; JP 2003518987 W Based on WO 2001049226
PRAI AU 2000-4965 20000106
IC ICM A61F009-00; A61F009-007; A61M005-00
ICS A61M005-158
AB WO 200149226 A UPAB: 20010829
NOVELTY - A plaque (5) positioned over a patient's eye, comprises an inner surface which contacts the anterior surface of the eye, and an outer surface positioned which faces away from the eye. The inner surface has surface area equivalent to the exposed surface of the eye. The plaque is further provided with one or more guide units (6b), for guiding a needle into the interior of eye (pars plana).

DETAILED DESCRIPTION - The guide units are placed at a distance from the plaque which corresponds to center of iris. The plaque has a pair of opposed retaining units directed and dimensioned to ensure retraction of eye lids, when the plaque is placed over the eyes. The plaque has a control unit on the outer surface which regulates the penetration of needle into the eye. INDEPENDENT CLAIMS are also included for the following:

(1) kit for use in intraocular injection of compound; and

(2) guiding and administering an intraocular composition into the interior of a patient's eye.

USE - Useful for intravitreal administration of therapeutic agents, for treating intraocular conditions such as variety of exudative, edematous and inflammatory retinopathies such as **macular degeneration**, diabetic retinopathy, diabetic **macular** edema, cystoid **macular** edema, uveitis, endophalmitis, retinal veno-occlusive disease, proliferative vitreo retinopathy, iritis, photodynamic therapy for **macular degeneration**, and also for application to aphakic eye.

ADVANTAGE - The plaque effectively immobilizes both the eye and eyelids during intraocular injection, prevents indentation of eye surface by penetration of needle and also allows correct angle of attack by needle, suitably at a distance from limbus and at suitable depth.

DESCRIPTION OF DRAWING(S) - The figure shows the illustration of the plaque in position over the eye with a needle being introduced through one of the guide unit.

Syringe 1
Needle 2
Plaque 5
Guide units 6b
Dwg.4/6

FS CPI GMPI
FA AB; GI; DCN
MC CPI: B11-C; B14-N03
TECH UPTX: 20010829
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Compound: The compound which is introduced into the eye through needle is anti-inflammatory steroid, non-steroidal anti-inflammatory agent, metalloproteinase inhibitor, anti-angiogenic agent, antioxidant, anti-cytokine agent, anti-sense RNA, gene transfer vector, anti-viral, anti-fungal, antibiotic, anti-proliferative agent, anti-metabolite, tyrosine kinase inhibitor or calcium channel blocker. The compound is 11-substituted-16alpha,17alpha-substituted methylenedioxy steroid, preferably triamcinolone acetonide, flucinolone acetonide or **anecortave acetate.**

L75 ANSWER 5 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-432457 [46] WPIX
CR 2001-425112 [45]; 2002-672690 [72]; 2004-051015 [05]
DNN N2001-320495 DNC C2001-130762
TI New ophthalmic drug delivery device with geometry that facilitates it implantation on an outer surface of the sclera beneath the inferior oblique muscle, with the drug disposed above the macula.
DC A96 B05 B07 P32 P34

IN YAACOBI, Y
PA (ALCO-N) ALCON UNIVERSAL LTD; (ALCO-N) ALCON INC; (YAAC-I) YAACOBI Y
CYC 37
PI WO 2001028474 A1 20010426 (200146)* EN 41 A61F009-00
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU BR CA CN JP KR MX PL TR US ZA
AU 2001010812 A 20010430 (200148)
US 6416777 B1 20020709 (200253) A61F002-14
EP 1221919 A1 20020717 (200254) EN A61F009-00
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
BR 2000014928 A 20021001 (200268) A61F009-00
KR 2002060206 A 20020716 (200305) A61F009-00
US 2003003129 A1 20030102 (200305) A61F002-00
CN 1376042 A 20021023 (200313) A61F009-00
JP 2003511205 W 20030325 (200330) 37 A61F009-007
ZA 2002001189 A 20030430 (200334)# 49 A61F000-00
AU 764226 B 20030814 (200363) A61F009-00
MX 2002002925 A1 20020801 (200367) A61F009-00
TW 539560 A 20030701 (200379) A61M035-00
US 6669950 B2 20031230 (200402) A61F002-14
AU 2003262099 A1 20031204 (200436) A61F009-00
US 2004131654 A1 20040708 (200445) A61F002-00
US 2004131655 A1 20040708 (200445) A61F002-00
ADT WO 2001028474 A1 WO 2000-US28187 20001012; AU 2001010812 A AU 2001-10812 20001012; US 6416777 B1 Provisional US 1999-160673P 19991021, US 2000-664790 20000919; EP 1221919 A1 EP 2000-972099 20001012, WO 2000-US28187 20001012; BR 2000014928 A BR 2000-14928 20001012, WO 2000-US28187 20001012; KR 2002060206 A KR 2002-705022 20020419; US 2003003129 A1 Provisional US 1999-160673P 19991021, Cont of US 2000-664790 20000919, US 2002-187006 20020701; CN 1376042 A CN 2000-813192 20001012; JP 2003511205 W WO 2000-US28187 20001012, JP 2001-531071 20001012; ZA 2002001189 A ZA 2002-1189 20020212; AU 764226 B AU 2001-10812 20001012; MX 2002002925 A1 WO 2000-US28187 20001012, MX 2002-2925 20020315; TW 539560 A TW 2000-122134 20001020; US 6669950 B2 Provisional US 1999-160673P 19991021, Cont of US 2000-664790 20000919, US 2002-187006 20020701; AU 2003262099 A1 AU 2003-262099 20031112; US 2004131654 A1 Provisional US 1999-160673P 19991021, Cont of US 2000-664790 20000919, Div ex US 2002-187006 20020701, US 2003-697141 20031030; US 2004131655 A1 Provisional US 1999-160673P 19991021, Cont of US 2000-664790 20000919, Div ex US 2002-187006 20020701, US 2003-697423 20031030
FDT AU 2001010812 A Based on WO 2001028474; EP 1221919 A1 Based on WO 2001028474; BR 2000014928 A Based on WO 2001028474; US 2003003129 A1 Cont of US 6416777; JP 2003511205 W Based on WO 2001028474; AU 764226 B Previous Publ. AU 2001010812, Based on WO 2001028474; MX 2002002925 A1 Based on WO 2001028474; US 6669950 B2 Cont of US 6416777; AU 2003262099 A1 Div ex AU 764226; US 2004131654 A1 Cont of US 6416777, Div ex US 6669950; US 2004131655 A1 Cont of US 6416777, Div ex US 6669950
PRAI US 2000-664790 20000919; US 1999-160673P 19991021;
US 2002-187006 20020701; ZA 2002-1189 20020212;
US 2003-697141 20031030; US 2003-697423 20031030
IC ICM A61F000-00; A61F002-00; A61F002-14; A61F009-00; A61F009-007; A61M035-00
ICS A61K009-00; A61M037-00
AB WO 200128474 A UPAB: 20040716
NOVELTY - Device for delivering drugs to the human eye (which has a sclera, an inferior oblique muscle and a **macula**), comprising a pharmaceutically active agent and a geometry that facilitates an implantation of the device on an outer surface of the sclera beneath the inferior oblique muscle, the active agent being disposed above the **macula**, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for delivering a pharmaceutically active agent to the human eye (which has a

sclera, an inferior oblique muscle and a **macula**), by providing:
(a) a drug delivery device comprising a pharmaceutically active agent; and
(b) disposing the device on an outer surface of the sclera, beneath the inferior oblique muscle, and with the active agent being disposed above the **macula.**
USE - The device is an implant for localized delivery of the pharmaceutically active agents to the posterior segment of the eye to combat age-related **macular degeneration** (**ARMD**), choroidal neovascularization (CNV), retinopathies, retinitis, uveitis, **macular**, edema, glaucoma and neuropathies. Furthermore because of their capability to deliver a wide variety of actives, they are useful in clinical studies to deliver ophthalmic agents that create a specific physical condition in a patient.
ADVANTAGE - The invention provides improved devices and methods for safe, effective, rate-controlled, localized delivery of a variety of actives to the eye. The surgical procedure for implanting such devices is safe, simple, quick and capable of being performed in an outpatient setting. The devices are easy and economical to manufacture.
Dwg.0/21
FS CPI GMPI
FA AB; DCN
MC CPI: A12-V01; A12-V03D; B01-C06; B07-D05; B10-B02A; B11-C03; B11-C04A; B14-N03
TECH UPTX: 20010815
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Device: The geometry is generally F-, L- or C-shaped. The device further comprises: (a) a body with a scleral surface for placement proximate the outer surface of the sclera and a well with an opening to the scleral surface; and (b) an inner core disposed in the well comprising the active agent. The body comprises a biocompatible, non-bioerodable material. The body can comprise a polymeric composition, preferably consisting of one or more of the following polymers: silicone (preferred), polyvinyl alcohol, ethylene vinyl acetate, polylactic acid, nylon, polypropylene, polycarbonate, cellulose, cellulose acetate, polyglycolic acid, polylactic glycolic, cellulose esters, polyethersulfone and acrylics. The body is impermeable to the active. The inner core is tablet and can be semi-solid form in which is disposed the active. The body comprises an orbital surface with a radius of curvature that facilitates implantation of the device below Tenon's capsule. The scleral surface has a radius of curvature which is equal to the radius of curvature of the human eye. The active is nepafenac or is selected from 4,9(11)-pregnadien-17alpha,21-diol-3,20-dione and 4,9(11)-pregnadien-17alpha,21-diol-3,20-dione-21-acetate, eliprodil. The drug delivery device comprises a retaining member extending from the body proximate the opening. The body comprises a notch for facilitating the accommodation of the inferior oblique muscle during device implantation.
ABEX UPTX: 20010815
EXAMPLE - None given.

L75 ANSWER 6 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-425112 [45] WPIX
CR 2001-432457 [46]; 2002-672690 [72]; 2004-051015 [05]
DNN N2001-315406 DNC C2001-128562
TI Implantable drug delivery device for ophthalmic drug delivery, comprises body having an internal surface for placement proximate a target tissue and a well having an opening to the internal surface, and an inner core disposed in the well.
DC A96 B01 B07 P32
IN YAACOBI, Y
PA (ALCO-N) ALCON UNIVERSAL LTD; (ALCO-N) ALCON INC
CYC 31
PI WO 2001028472 A1 20010426 (200145)* EN 53 A61F009-00
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: AU BR CA CN JP KR MX PL TR US ZA

AU 2000073733	A	20010430	(200148)			
EP 1221917	A1	20020717	(200254)	EN		A61F009-00
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE						
BR 2000014929	A	20021001	(200268)			A61F009-00
KR 2002059630	A	20020713	(200306)			A61F009-00
JP 2003515528	W	20030507	(200331)		32	A61K009-00
ZA 2002001188	A	20030430	(200334)		43	A61F000-00
MX 2002002338	A1	20020801	(200367)			A61F009-00
AU 768400	B	20031211	(200404)			A61F009-00
TW 555575	A	20031001	(200423)			A61M037-00

ADT WO 2001028472 A1 WO 2000-US24983 20000912; AU 2000073733 A AU 2000-73733 20000912; EP 1221917 A1 EP 2000-961836 20000912, WO 2000-US24983 20000912; BR 2000014929 A BR 2000-14929 20000912, WO 2000-US24983 20000912; KR 2002059630 A KR 2002-705020 20020419; JP 2003515528 W WO 2000-US24983 20000912, JP 2001-531069 20000912; ZA 2002001188 A ZA 2002-1188 20020212; MX 2002002338 A1 WO 2000-US24983 20000912, MX 2002-2338 20020304; AU 768400 B AU 2000-73733 20000912; TW 555575 A TW 2000-120788 20001005

FDT AU 2000073733 A Based on WO 2001028472; EP 1221917 A1 Based on WO 2001028472; BR 2000014929 A Based on WO 2001028472; JP 2003515528 W Based on WO 2001028472; MX 2002002338 A1 Based on WO 2001028472; AU 768400 B Previous Publ. AU 2000073733, Based on WO 2001028472

PRAI US 1999-160673P 19991021

IC ICM A61F000-00; A61F009-00; A61K009-00; A61M037-00
ICS A61F009-007; A61K009-20; A61K031-575; A61K045-00; A61K047-30; A61K047-32; A61K047-34; A61K047-38; A61P027-02

AB WO 200128472 A UPAB: 20040405
NOVELTY - A drug delivery device (I), comprising: (a) a body having an internal surface for placement proximate a target tissue and a well having an opening to the internal surface; and (b) an inner core disposed in the well comprising a pharmaceutically active agent.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) delivering a pharmaceutically active agent to a target tissue within a body, comprising:

(a) providing a drug delivery device (I); and

(b) disposing the device within the body so that the pharmaceutically active agent is in communication with the target tissue through the opening;

(2) an ophthalmic drug delivery device, comprising:

(a) a body having a scleral surface for placement proximate a sclera and a well having an opening to the scleral surface; and

(b) an inner core disposed in the well comprising a pharinaceutically active agent;

(3) delivering a pharmaceutically active agent to an eye, the eye having a sclera, comprising the steps of:

(i) providing a drug delivery device comprising:

(a) a body having a scleral surface and a well having an opening to the scieral surface; and

(b) an inner core disposed in the well comprising a pharmaceutically active agent; and

(ii) disposing the device with in the eye so that the pharmaceutically active agent is in communication with the sclera through the opening; and

(4) delivering a pharmaceutically active agent to the eye, the eye having a sclera, a Tenon's capsule, and a macula, comprising the steps of:

(a) providing a drug delivery device comprising a body having a pharmaceutically active agent disposed; and

(b) disposing the device on an outer surface of the sclera, below the Tenon's capsule, and proximate the macula.

USE - Implantable drug delivery device for ophthalmic drug delivery, especially for localized delivery of pharmaceutically active agents to the posterior segment of the eye to combat **ARMD**, CNV, retinopathies,

retinitis, uvetitis, macular edema and glaucoma.
ADVANTAGE - The device is safe, effective, rate controlled, and easy and economical to manufacture.
DESCRIPTION OF DRAWING(S) - Figure is a sectional view of drug delivery device.
drug delivery device 10
body 12
internal surface 14
external surface 16
proximal end 18
distal end 20
well 22
opening 24
inner core 26
retaining member 28
Dwg.1/7
FS CPI GMPI
FA AB; GI; DCN
MC CPI: A12-V02A; B01-C06; B04-C03; B07-D05; B11-C04A; B14-C03; B14-N03; B14-N04
TECH UPTX: 20010813
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: The drug delivery device of body comprises a biocompatible, non-bioerodable material. The body comprises a polymeric composition.
Preferred Device: The drug delivery device further comprising a retaining member extending from the body proximate the opening. The inner core is a tablet, and comprises a hydrogel, the pharmaceutically active agent is disposed within the hydrogel. The body is impermeable to the pharmaceutically active agent. The internal surface has a geometry that mates with a surface of the target tissue. The device is surgically implantable into a body. The pharmaceutically active agent comprises a compound selected from 4,9(11)-Pregnadien17alpha,21-diol-3,20-dione and 4,9(11)-Pregnadien-17alpha,21-diol-3,20-dione-21-acetate. The pharmaceutically active agent comprises eliprodil.
Preferred Method: The method comprising the step of delivering a pharmaceutically effective amount of the pharmaceutically active agent to the target tissue for a period of time. The scleral surface has a geometry that mates with the sclera. The device is surgically implantable into an eye, and further comprising an orbital surface having at least one tapered surface that facilitates implantation of the device. The eye is a human eye having a macula, and the disposing step comprises disposing the device generally above the macula. The human eye having a choroid and a retina, and further comprising the step of delivering a pharmaceutically effective amount of the pharmaceutically active agent through the sclera and the choroid and to the retina over a period of time.

TECHNOLOGY FOCUS - POLYMERS - Preferred Composition: The polymeric composition comprises one or more polymers selected from silicone, polyvinyl alcohol, ethylene vinyl acetate, polylactic acid, nylon, polypropylene, polycarbonate, cellulose, cellulose acetate, polyglycolic acid, polylactic glycolic acid, cellulose esters, polyethersulfone, and acrylics.

=> d 3 5 6 dcn

L76 ANSWER 3 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
M5 *04* DCN: **RA0EF8-K**; **RA0EF8-T**; **RA0EF8-M**
M5 *05* DCN: R00141-K; R00141-T; R00141-M
M5 *06* DCN: R06358-K; R06358-T; R06358-M; R06359-K; R06359-T; R06359-M
M5 *07* DCN: 0071-89406-K; 0071-89406-T; 0071-89406-M
M5 *08* DCN: 0071-89403-K; 0071-89403-T; 0071-89403-M
M5 *09* DCN: 0071-89401-K; 0071-89401-T; 0071-89401-M

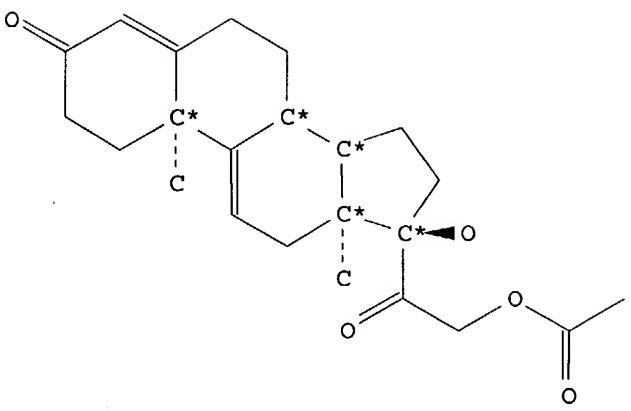
M5 *10* DCN: 0071-89409-K; 0071-89409-T; 0071-89409-M
M5 *11* DCN: 0071-89408-K; 0071-89408-T; 0071-89408-M
M5 *12* DCN: 0071-89404-K; 0071-89404-T; 0071-89404-M
M5 *13* DCN: 0071-89407-K; 0071-89407-T; 0071-89407-M
M5 *14* DCN: 0071-89405-K; 0071-89405-T; 0071-89405-M
M5 *15* DCN: 0071-89402-K; 0071-89402-T; 0071-89402-M

L76 ANSWER 5 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
M2 *01* DCN: RA059O-K; RA059O-T; RA059O-M
M2 *02* DCN: R04971-K; R04971-T; R04971-M
M2 *03* DCN: RA01ZO-K; RA01ZO-T; RA01ZO-M
M2 *04* DCN: 0033-63609-K; 0033-63609-T; 0033-63609-M
M2 *05* DCN: 0033-63608-K; 0033-63608-T; 0033-63608-M
M2 *06* DCN: 0033-63607-K; 0033-63607-T; 0033-63607-M
M5 *07* DCN: **RA0EF8-K; RA0EF8-T; RA0EF8-M**
M5 *08* DCN: 0033-63606-K; 0033-63606-T; 0033-63606-M
M5 *09* DCN: 0033-63605-K; 0033-63605-T; 0033-63605-M
M5 *10* DCN: 0033-63604-K; 0033-63604-T; 0033-63604-M
M5 *11* DCN: 0033-63603-K; 0033-63603-T; 0033-63603-M
M5 *12* DCN: 0033-63602-K; 0033-63602-T; 0033-63602-M
M5 *13* DCN: 0033-63601-K; 0033-63601-T; 0033-63601-M

L76 ANSWER 6 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
M2 *14* DCN: 0004-46908-K; 0004-46908-U
M5 *01* DCN: RA0EF4-K; RA0EF4-U
M5 *02* DCN: RA0EF5-K; RA0EF5-U
M5 *03* DCN: RA0EF6-K; RA0EF6-U
M5 *04* DCN: RA0EF7-K; RA0EF7-U
M5 *05* DCN: **RA0EF8-K; RA0EF8-U**
M5 *06* DCN: RA0EF9-K; RA0EF9-U
M5 *07* DCN: 0004-46901-K; 0004-46901-U
M5 *08* DCN: 0004-46902-K; 0004-46902-U
M5 *09* DCN: 0004-46903-K; 0004-46903-U
M5 *10* DCN: 0004-46904-K; 0004-46904-U
M5 *11* DCN: 0004-46905-K; 0004-46905-U
M5 *12* DCN: 0004-46906-K; 0004-46906-U
M5 *13* DCN: 0004-46907-K; 0004-46907-U

=> d l70 all

L70 ANSWER 1 OF 1 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN.S DCR-219509
DCSE 219509-1-0-0
CN.P ANECORTAVE
CN.S 4,9(11)-Pregnadien-17alpha,21-Diol-3,20-Dione-21-Acetate; Acetic acid 2-(17-hydroxy-10,13-dimethyl-3-oxo-2,3,6,7,8,10,12,13,14,15,16,17-dodecahydro-1H-cyclopenta[a]phenanthren-17-yl)-2-oxo-ethyl ester
SY AL-3789; **ANECORTAVE**



MF C23 H30 O5
SMF C23 H30 O5 *1; TOTAL *1; TYPE *1
MW 386.4926
SDCN RA0EF8
CC STEROIDS
SMIL CC(=O)OCC(=O)C1(O)CCC2C3CCC4=CC(=O)CCC4(C)C3=CCC21C
ISMI CC(=O)OCC(=O)[C@@]1(O)CC[C@H]2[C@@H]3CCC4=CC(=O)CC[C@]4(C)C3=CC[C@@]21C

=> d l76 all abeq tech abex tot

L76 ANSWER 1 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-863951 [80] WPIX
DNC C2003-244196
TI Treatment and/or prevention of central nervous system disorders and/or states involves administration of a pharmaceutical composition by an ocular route of drug delivery.
DC A96 B05 B07 D22
IN ABDULRAZIK, M
PA (ABDU-I) ABDULRAZIK M
CYC 1
PI US 2003181354 A1 20030925 (200380)* 17 A61K031-00
ADT US 2003181354 A1 US 2003-354173 20030130
PRAI IL 2002-147921 20020131
IC ICM A61K031-00
AB US2003181354 A UPAB: 20031211
NOVELTY - Treatment and/or prevention of central nervous system disorders and/or states involves administration of a pharmaceutical composition (A) by an ocular route of drug delivery.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for method (M) for the treatment of migraines in humans involving:
(a) administering a pharmaceutical composition (A') by an ocular route of drug delivery; or
(b) administering an established anti-migraine therapeutic agent by an ocular route of drug delivery.
ACTIVITY - CNS-Gen.; Vasotropic; Tranquilizer; Analgesic; Antimigraine; Neuroprotective; Anticonvulsant; Antiparkinsonian; Nootropic; Muscular-Gen.; Cytostatic; Antibacterial; Antiinflammatory; Antidepressant; Neuroleptic; Antiaddictive; Eating-disorder-Gen.; Anorectic; Hypotensive; Auditory; Ophthalmological; Antiangiogenic; Cerebroprotective; Immunosuppressive; Antiarthritic; Antiarteriosclerotic; Anabolic; Immunomodulator; Uropathic; Sedative; Endocrine-Gen.; Hypnotic; Antimicrobial; Antialcoholic; Antismoking.
A 48-year old female patient with a history of migraine, and right eye primary open angle glaucoma was prescribed with brimonidine tartrate

(0.2%) as a second topical antiglaucoma agent. The patient reported a substantial relief of migraine related symptoms.

MECHANISM OF ACTION - None given.

USE - For the treatment and/or prevention of central nervous system disorders and/or states in human or animal e.g. central nervous system ischemia, central nervous system reperfusion injury, spinal ischemia, central nervous system trauma, crushed or compressed optic nerve, headache, migraine, pain, multiple sclerosis, optic neuritis, optic neuropathies, ocular glaucomatous damage, epilepsy, convulsions, neurodegenerative diseases, Parkinson's disease, Alzheimer's disease, ataxias, dystonias, movement disorders, choreas, intracranial tumors, intracranial metastasis, intracranial infections, meningitis, central nervous system states in need of cognition enhancement, memory disorders, depression, avoidant personality disorder, anxiety, panic disorder, obsessive-compulsive disorders, phobias, impulsive disorders, cognitive disorders, mood disorders, psychoses, schizophrenia, drug abuse, chemical dependencies, drugs tolerance or withdrawal, posttraumatic stress syndrome, eating disorders, obesity premature ejaculation, hypertension, aminoglycoside antibiotics-induced hearing loss, central nervous system drug-induced disorders and states, N-methyl-D-aspartate-induced neurodegeneration, glutamate induced excitotoxic effects on nerve cells, central nervous system metabolic disorders and states, central nervous system deficiency disorders, central nervous system disorders and states amenable to neuropeptides therapy, central nervous system disorders and states amenable to neurotrophic factors therapy, central nervous system disorders and states amenable to neuroprotective therapy, central nervous system mediated ocular glaucomatous damage, autoimmune glaucoma, central nervous system disorders and states amenable to gene-therapy, surgically-induced inflammation, trauma-induced inflammation, angiogenesis-related disorder, hypoproliferative diseases, brain or spinal cord disease, disorder or injury, conditions which can lead to excessive glutamate release, conditions which can lead to neurodegeneration, stroke, impaired blood flow in neuronal tissue, septic or traumatic shock, hemorrhage shock, arthritis, arteriosclerosis, conditions which can lead to bursting of the myelin sheath around nerves, senile dementia, Huntington's disease, Lou Gehrig's disease (ALS), addictive disorders to at least one of alcohol, nicotine, and other psychoactive substance, adjustment disorder, age-associated learning and mental disorder, anorexia nervosa, apathy, attention-deficit disorder due to general medical conditions, attention-deficit hyperactivity disorder, bipolar disorder, bulimia nervosa, chronic fatigue syndrome, chronic or acute stress, conduct disorder, cyclothymic disorder, dizziness, dysthymic disorder, fibromyalgia and other somatoform disorders, incontinence, inhalation disorder, insomnia, intoxication disorder, obesity, peripheral neuropathy, premenstrual dysphoric disorder, psychotic disorder, seasonal affective disorder, sexual dysfunction, sleep disorder (e.g. narcolepsy and enuresis), specific developmental disorder, TIC disorders (e.g. Tourette's disease and withdrawal syndrome) (claimed).

ADVANTAGE - The method achieves effective CNS target site concentrations of the drugs, while limiting systemic exposure and distribution of the drug to peripheral sites of action. Thus lessens unwanted side effects and the potential for toxicity.

Dwg.0/8

FS CPI

FA AB; DCN

MC CPI: A12-V01; B01-C03; B06-D06; B06-E03; B06-F03; B07-D09; B07-E01; B07-F02; B09-D01; B10-A17; B10-D03; B10-E04; B14-C01; B14-C03; B14-C09; B14-D01; B14-E11; B14-F02C; B14-F02D; B14-F02D1; B14-F05; B14-H01B; B14-J01; B14-J01A3; B14-J01B3; B14-J05; B14-J05C; B14-J07; B14-L01; B14-M01A; B14-M01B; B14-M01C; B14-N03; B14-N07D; B14-N09; B14-N16; B14-P02; B14-S01; B14-S06; B14-S07; D09-A; D09-C01

TECH UPTX: 20031211

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: (A) comprises

N-methyl-D-aspartate receptor antagonist (preferably memantine); alpha-2 adrenoreceptor agonist (preferably alpha-2 adrenoreceptor subtype specific agonist) (preferably brimonidine); beta-blocker; established anti-cancer therapeutics, their derivatives, prodrugs and/or codrugs; established anti-Parkinsonian therapeutics or their combinations; recombinant adeno-associated virus, other established gene-therapy vectors and/or other gene delivery systems; zinc derivatives, magnesium derivatives, vitamins and/or multi-vitamins; established ophthalmic therapeutics, their derivatives, prodrugs and/or codrugs; prostaglandin analogues, their derivatives, prodrugs and/or codrugs; prostamid receptor agonist (preferably bimatoprost); cannabinoid receptors agonists; steroid (preferably angiostatic steroid, especially **anecortave**); imino-imidazoline (preferably clonidine or apraclonidine); catecholamine; alpha-2 adrenergic agonist (preferably quinoxaline). The alpha-2 adrenoreceptor agonist is selected from imidazoline (preferably naphazoline, xymetazoline, tetrahydrozoline or tramazoline), imidazole (preferably detomidine, medetomidine or dexmedetomidine), azepine (preferably B-HT 920 (6-allyl-2-amino-5,6,7,8-tetrahydro-4H-thiazolo(4,5-d)-azepine) or B-HT 933), thiazines (preferably xylazine), thiazine (preferably xylazine), oxazoline (preferably rilmenidine), or guanidine (preferably guanabenz or guanfacine). Quinoxaline is selected from (2-imidazolin-2-ylamino) quinoxaline, 5-halide-6-(2-imidazolin-2-ylamino) quinoxaline or tartrate of 5-bromo-6-(2-imidazolin-2-ylamino) quinoxaline. The prostaglandin analogue is selected from latanoprost, unoprostone, travaprost or bimatoprost. (A') comprises alpha-2 adrenoceptor antagonist and also includes brimonidine tartrate.

Preferred Method: Method (A) further involves administering an established anti-migraine therapeutic agent in combination with (A'). The established anti-migraine therapeutic agent is administered systemically or ocularly. Brimonidine tartrate is administered ocularly in a composition containing (0.0001 - 9)% brimonidine tartrate.

ABEX UPTX: 20031211

ADMINISTRATION - The ocular route of drug delivery involves delivery by eye-drop, suspension, ointment, gel, hydrogel and viscosified solution system, gel-forming system, lotion, spray, liposome, emulsion, strip, therapeutic contact lenses, membrane-bound devises, collagen shield, insert, polymeric dosing system, rod-like insert, iontophoresis, anterior chamber dosing, sub-conjunctival dosing or implant, subtenon dosing or implant, retrobulbar dosing or implant, peribulbar dosing or implant, trans-septal dosing or implant, choroidal dosing or implant, ciliary body dosing or implant, subretinal dosing or implant, intra-vitreal dosing or implant, intraocular implantable or injected sustained release system, encapsulated cell technology dosing system, transscleral drug delivery system, optic nerve related dosing system, infusion to ocular tissue via a pump-catheter system, drug incorporation in surgical irrigating solution or ocular dosing of gene-therapy vector (claimed).

EXAMPLE - No relevant example given.

L76 ANSWER 2 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-221819 [21] WPIX
DNN N2003-176875 DNC C2003-056583
TI Ocular iontophoretic device for non-invasive delivery of a steroid composition to the eye, is useful for treating inflammatory or neovascularization conditions.
DC B01 B07 D22 P34 S05
IN LLOYD, L B; PARKINSON, T M; SZLEK, M
PA (LLOY-I) LLOYD L B; (PARK-I) PARKINSON T M; (SZLE-I) SZLEK M; (IOME-N) IOMED INC
CYC 100
PI WO 2003008036 A2 20030130 (200321)* EN 26 A61N000-00
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW

US 2003023228 A1 20030130 (200325) A61M031-00
AU 2002316723 A1 20030303 (200452) A61N000-00

ADT WO 2003008036 A2 WO 2002-US22859 20020719; US 2003023228 A1 US 2001-910443 20010720; AU 2002316723 A1 AU 2002-316723 20020719
FDT AU 2002316723 A1 Based on WO 2003008036
PRAI US 2001-910443 20010720
IC ICM A61M031-00; A61N000-00
AB WO2003008036 A UPAB: 20030328
NOVELTY - An ocular iontophoretic device for non-invasive delivery of a steroid composition to the eye, comprises an active electrode assembly associated with a matrix, where the matrix includes a corticosteroid, **anecortave** phosphate steroid or amino sterole composition, particularly dexamethasone, for treating inflammatory and/or neovascularization conditions.

ACTIVITY - Ophthalmological; Antiinflammatory.

MECHANISM OF ACTION - None given.

USE - The device is for the delivery of steroid compositions to the eye, especially in the treatment of inflammatory or neovascularization conditions.

ADVANTAGE - Compared to previous delivery methods, the device enables a generally painless, non-invasive and deep delivery of a steroid composition. The composition is locally delivered to an affected area of the eye at an effective, therapeutic level.

Dwg.0/3

FS CPI EPI GMPI
FA AB; DCN
MC CPI: B01-B02; B11-C04; B12-M10A; B14-C03; B14-F02F; B14-N03; D09-C04
EPI: S05-A07
TECH UPTX: 20030328
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: The dexamethasone composition has molecular weight 400-600. Preferred compositions include dexamethasone sodium phosphate, and esters, e.g. 9-fluoro 11beta,17-dihydroxy-16alpha-methyl-21-(phosphonooxy)pregna-1,4-diene 3,20-dione disodium salt. The composition comprises 0.5-4, preferably 1 wt.% of compound. The buffer pH is 6-8.5, preferably 7.4. Preferred Device: The device may further comprise a counter electrode assembly, completing an electrical circuit between the active electrode assembly and an energy source, and an energy source for generating electrical potential difference. The active electrode assembly includes an open-faced or high current density electrode. The device is positioned on the conjunctival surface in a region of a pars planum and/or insertions of an anterior cilliary artery.
ABEX UPTX: 20030328
ADMINISTRATION - Administration is into the vitreous humor, retina, choroids, circulation of the retina, circulation of the choroid, or sclera. The composition is iontophoretically delivered at 0.5-4 mA for 5-20 minutes.

L76 ANSWER 3 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-643247 [69] WPIX
DNC C2004-014126
TI Composition useful for controlling and lowering intraoccular pressure comprises an angiostatic agent and at least one intraoccular pressure lowering compound.
DC B01
IN CLARK, A F
PA (ALCO-N) ALCON LAB INC; (ALCO-N) ALCON MFG LTD
CYC 30
PI WO 2002040030 A1 20020523 (200269)* EN 19 A61K031-56

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
W: AU BR CA CN JP KR MX PL US ZA
AU 2001017709 A 20020527 (200269) A61K031-56
EP 1341541 A1 20030910 (200367) EN A61K031-56
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE TR
JP 2004522711 W 20040729 (200452) 36 A61K045-06

ADT WO 2002040030 A1 WO 2000-US31557 20001116; AU 2001017709 A WO 2000-US31557 20001116, AU 2001-17709 20001116; EP 1341541 A1 EP 2000-980450 20001116, WO 2000-US31557 20001116; JP 2004522711 W WO 2000-US31557 20001116, JP 2002-542403 20001116

FDT AU 2001017709 A Based on WO 2002040030; EP 1341541 A1 Based on WO 2002040030; JP 2004522711 W Based on WO 2002040030

PRAI WO 2000-US31557 20001116

IC ICM A61K031-56; A61K045-06
ICS A61K031-138; A61K031-5377; A61K031-5575; A61K031-57; A61P009-00; A61P027-02

AB WO 200240030 A UPAB: 20040429
NOVELTY - A composition comprises an angiostatic agent (I) or (II) and at least one other compound (III) which lowers intraoccular pressure (IOP).
ACTIVITY - Ophthalmological; Hypotensive.
MECHANISM OF ACTION - Glycosaminoglycan Inhibitor.
No biological data given.
USE - For lowering and controlling intraoccular pressure (IOP) (claimed), and in the treatment of glaucoma and ocular hypertension.
ADVANTAGE - The composition provides effective, long duration control of intraoccular pressure (IOP) with less IOP spiking.
Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B01-A02; B01-B03; B01-B04; B01-C07; B07-D09; B07-E03; B07-F01; B10-B03B; B14-F02B; B14-N03

TECH UPTX: 20040429
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: The angiostatic agent is a compound of formula (I), (II) or their salts.
R1 = H, -CH3 or -C2H5;
R2 = F, 9-11C double bond, 9-11C epoxy, H or Cl;
R3 = H, OR26, OC(=O)R27, halo, 9-11C double bond, 9-11C epoxy, =O, -OH, -O-1-12C alkyl, -OC(=O)-1-12C alkyl, -OC(=O)-Ar, -OC(=O)N(R)2 or -OC(=O)OR7;
Ar = furyl, thienyl, pyrrolyl or pyridyl (all optionally substituted with 1-2 1-4C alkyl) or (CH2)f-phenyl (phenyl is optionally substituted with 1-3 T);
T = Cl, F, Br, 1-3C alkyl, 1-3C alkoxy, 1-3C thioalkoxy, Cl3C-, F3C-, -NH2 or -NHCOCH3;
R = H, 1-4C alkyl or phenyl;
R7 = Ar or 1-12C alkyl;
R4 = H, CH3, Cl or F;
R5 = R4, OH, Br, phenyl, vinyl or allyl;
R6 = H or CH3;
R9 = CH2CH2OR26, CH2CH2OC(=O)R27, H, OH, CH3, F, =CH2, CH2C(=O)OR28, OR26, O(C=O)R27 or O(C=O)CH2(C=O)OR26;
R10 = -CCH, -CH=CH2, halo, CN, N3, OR26, OC(=O)R27, H, OH, CH3 or a double bond between C-16 and C-17;
R12, R14 = H; or
R12+R1, R12+R14 = double bond;
R13 = halo, OR26, OC(=O)R27, NH2, NHR26, NHC(=O)R27, N(R26)2, NC(=O)R27, N3, H, -OH, =O, -O-P(=O)(OH)2 or -O-C(=O)-(CH2)t-COOH;
t = 2-6;
R15 = H, =O or -OH;
R10+R23 = cyclic phosphate;
R23 = -OH, O-C(=O)-R11, -OP(O)-(OH)2 or -O-C(=O)-(CH2)tCOOH;
R11 = -Y-(CH2)n-X-(CH2)m-SO3H, -Y'-(CH2)p-X'-(CH2)q-NR16R17 or -Z(CH2)r-Q;
Y, Z = bond or -O-;

Y' = bond, -O- or -S-;
X, X' = bond, -CON(R18)-, -N(R18)CO-, -O-, -S-, -S(O)- or -S(O2)-;
R18 = H or 1-4C alkyl;
R16, R17 = 1-4C lower alkyl optionally substituted by OH; or
NR16R17 = monocyclic heterocycle selected from pyrrolidino, piperidino, (thio)morpholino, piperazino or N(1-4C lower alkyl)-piperazino;
n = 4-9;
m, q = 1-5;
p, r = 2-9;
Q = -R19-CH2COOH, -CO-COOH or CON(R21)CH(R22)COOH;
R19 = -S-, -S(O)-, -S(O)2, -S(O)2N(R20)- or N(R20)SO2-;
R20 = H or 1-4C lower alkyl;
R21 = H or CH3;
R22 = H, CH3, -CH2COOH, -CH2CH2COOH, -CH2OH, -CH2SH, -CH2CH2SCH3 or -CH2Ph-OH (where Ph-OH is para hydroxyphenyl); or
R21+R22 = -CH2CH2CH2-; or
-N(R21)CH(R22)COOH = -NHCH2CONHCH2COOH;
R24 = CH, C1-C2 double bond, or O;
R25 = C(R15)CH2-R23, OH, OR26, OC(=O)R27, R26, COOH, C(=O)OR26, CHOHCH2OH, CHOHCH2OR26, CHOHCH2OC(=O)R27, CH2CH2OH, CH2CH2OR26, CH2CH2OC(=O)R27, CH2CN, CH2N3, CH2NH2, CH2NHR26, CH2N(R26)2, CH2OH, CH2OR26, CH2O(C=O)R27, CH2O(P=O)(OH)2, CH2O(P=O)(OR26)2, CH2SH, CH2S-R26, CH2SC(=O)R27, CH2NC(=O)R27, C(=O)CHR28OH, C(=O)CHR28OR26, or C(=O)CHR28OC(=O)R27; or
R10+R25 = C(R28)2 that is an optionally alkyl substituted methylene group;
R26 = 1-6C (optionally branched alkyl, cycloalkyl, haloalkyl, aralkyl or aryl);
R27 = R26+OR26; and
R28 = H or 1-6C (optionally branched alkyl or cycloalkyl);
provided that the total number of carbon atoms in R20 and (CH2)r is at least 10; when R21 is CH3, R22 is H. (III) Is selected from miotics, sympathomimetics, beta-blocker (preferably timolol, betaxolol or levobetaxolol), carbonic anhydrase inhibitors or prostaglandins.

ABEX UPTX: 20040429

SPECIFIC COMPOUNDS - Use of 4,9(11) Pregnadien-17,21-diol-21-acetate (Ia) as the angiostatic agent is specifically claimed.

ADMINISTRATION - The composition is administered topically to the affected eye, 1-2 drops, 1-4 times per day.

EXAMPLE - A composition comprised of (weight%): timolol maleate (0.68), 4,9(11) pregnadien-17,21-diol-3; 20-dione-21-acetate (1), mannitol (2.4), sodium chloride (0.4), Carbopol 974P (RTM; drug carrier substance) (0.5), polysorbate 80 (0.05), edetate disodium (0.01), benzalkonium chloride (0.01), NaOH (to pH 7.4) and purified water (balance to 100 ml).

L76 ANSWER 4 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-627225 [67] WPIX
DNN N2004-028639 DNC C2004-012568
TI Reduction or prevention of transplant rejection in an eye involves use of bioerodible drug delivery system comprising an immunosuppressive agent and a bioerodible polymer.
DC A96 B05 B07 D22 P32 P34
IN WONG, V G
PA (OCUL-N) OCULEX PHARM INC; (ALLR) ALLERGAN INC; (WONG-I) WONG V G
CYC 100
PI WO 2002043785 A2 20020606 (200267)* EN 33 A61L027-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2002036495 A 20020611 (200267) A61L027-00

US 2002182185 A1 20021205 (200301) A61K045-00
EP 1339438 A2 20030903 (200365) EN A61L027-54
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
BR 2001015772 A 20040113 (200409) A61L027-00
US 6699493 B2 20040302 (200417) A61F002-14
JP 2004514702 W 20040520 (200434) 64 A61K045-00
US 2004137034 A1 20040715 (200447) A61F002-00
JP 2004210798 A 20040729 (200450) 23 A61K031-573

ADT WO 2002043785 A2 WO 2001-US44481 20011128; AU 2002036495 A AU 2002-36495 20011128; US 2002182185 A1 Provisional US 2000-250023P 20001129, Provisional US 2001-298253P 20010612, US 2001-997094 20011128; EP 1339438 A2 EP 2001-986027 20011128, WO 2001-US44481 20011128; BR 2001015772 A BR 2001-15772 20011128, WO 2001-US44481 20011128; US 6699493 B2 Provisional US 2000-250023P 20001129, Provisional US 2001-298253P 20010612, US 2001-997094 20011128; JP 2004514702 W WO 2001-US44481 20011128, JP 2002-545755 20011128; US 2004137034 A1 Provisional US 2000-250023P 20001129, Provisional US 2001-298253P 20010612, Cont of US 2001-997094 20011128, US 2003-744560 20031222; JP 2004210798 A Div ex JP 2002-545755 20011128, JP 2004-121618 20040416

FDT AU 2002036495 A Based on WO 2002043785; EP 1339438 A2 Based on WO 2002043785; BR 2001015772 A Based on WO 2002043785; JP 2004514702 W Based on WO 2002043785; US 2004137034 A1 Cont of US 6699493

PRAI US 2001-298253P 20010612; US 2000-250023P 20001129;
US 2001-997094 20011128; US 2003-744560 20031222

IC ICM A61F002-00; A61F002-14; A61K031-573; A61K045-00; A61L027-00; A61L027-54
ICS A01N025-10; A61K009-00; A61K031-4745; A61K031-522; A61K031-525; A61K031-57; A61K038-00; A61K038-13; A61K047-30; A61K047-32; A61K047-34; A61K047-38; A61P027-02; A61P037-06; A61P041-00; A61P043-00

AB WO 200243785 A UPAB: 20040608
NOVELTY - Reduction or prevention of transplant rejection in an eye of an individual involves:
(a) performing an ocular transplant procedure on the eye and
(b) placing in the eye a bioerodible drug delivery system (I) comprising an immunosuppressive agent (Ia) and a bioerodible polymer (Ib).
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a kit comprising (I) and instructions for use. (I) is designed to be implanted in the eye.
ACTIVITY - Immunosuppressive; ophthalmological;
MECHANISM OF ACTION - None given.
USE - In the manufacture of bioerodible drug delivery system for reducing or preventing transplant rejection in an eye of an individual, e.g. human (claimed).
ADVANTAGE - The drug delivery system is made of a biodegradable polymer matrix which can release drug loads over various programmed time periods.
Dwg.0/0

FS CPI GMPI
FA AB; DCN
MC CPI: A05-E02; A12-V01; A12-V02A; B01-B02; B01-C04; B02-C; B04-C02A2; B04-C03C; B06-D02; B06-D06; B06-D09; B06-E05; B07-A02A; B07-D04B; B07-D09; B07-D12; B07-D13; B10-A17; B12-M10; B14-G02; B14-G02C; B14-N03; D09-C01

TECH UPTX: 20040426
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method: The method involves implanting into the eye a solid body comprising particles of (Ia) entrapped within (Ib). (Ia) is released from the solid body by erosion of (Ib). The ocular transplant procedure is a retinal pigment epithelium (RPE) transplant or a cornea transplant. (I) is placed in the anterior chamber or vitreous cavity of the eye.
Preferred Delivery System: (I) comprises (wt.%):

(i) dexamethasone or cyclosporin A (50, preferably 60) and PLGA (40, preferably 50) or
(ii) dexamethasone or cyclosporin A (50), hydroxy propyl methyl cellulose (HPMC) (15) and PLGA (35).

TECHNOLOGY FOCUS - POLYMERS - Preferred Components: (Ib) is a polymer or polylactic acid polyglycolic acid (PLGA) copolymer. The implant further comprises (HPMC) (15 wt.%).

ABEX UPTX: 20040426

SPECIFIC COMPOUNDS - Dexamethasone, cyclosporin A, azathioprine, brequinar, gusperimus, 6-mercaptopurine, mizoribine, rapamycin, (FK-506)(tacrolimus), denopterin, edatrexate, methotrexate, piritrexim, pteropterin, Tomudex, trimetrexate, cladribine, fludarabine, 6-mercaptopurine, thiamiprine, thiaguanine, ancitabine, azacitidine, 6-azauridine, carmofur, cytarabine, doxifluridine, emitefur, enocitabine, floxuridine, fluorouracil, gemcitabine, egafur, fluocinolone, triaminolone, **anecortave acetate**, fluorometholone, medrysone and prednisolone are specifically claimed as (Ia).

ADMINISTRATION - (I) is administered via intraocular implants for at least about 5 days.

EXAMPLE - Dexamethasone powder (2100 mg) was mixed with 50/50 polylactic acid polyglycolic acid (PLGA) (900 mg) at ambient temperature. A small Teflon tube was filled with the mixture (900 - 1100 mug) and placed directly on the die cavity. The powder was pressed using a tablet press, ejected and removed to obtain a pellet (approximately 2 mm x 0.75 mm). Release of dexamethasone from DEXPS DDS system was measured. The concentration values were used to calculate the cumulative release and showed that % total release of dexamethasone on day 1 and day 35 was 10.1 and 88.1 respectively.

L76 ANSWER 5 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-167739 [17] WPIX
DNC C2001-049955
TI Composition useful in treatment of glaucoma and ocular hypertension comprises angiostatic steroid compound in combination with intraocular pressure lowering agent.
DC B01
IN CLARK, A F
PA (ALCO-N) ALCON LAB INC
CYC 1
PI US 6172054 B1 20010109 (200117)* 7 A61K031-56
ADT US 6172054 B1 US 1995-491005 19950615
PRAI US 1995-491005 19950615
IC ICM A61K031-56
AB US 6172054 B UPAB: 20010328
NOVELTY - Composition comprises an angiostatic steroid compound (I) or (II) in combination with an intraocular pressure lowering agent (III).

DETAILED DESCRIPTION - Composition comprises an angiostatic steroid compound of formula (I) or (II) or their salts and at least one intraocular pressure (IOP) lowering compound (III) comprising miotics, sympathomimetics, beta -blockers, carbonic anhydrase inhibitors and/or prostaglandins.

R1 = H, beta -methyl or beta -ethyl;

R2 = F, 9-11C double bond, 9-11C 1-epoxy, H or Cl;

R3 = H, OR26, OC(=O)R27, halo, 9-11C double bond, 9C-Cl, 1-epoxy, =O, OH, 1-12C alkoxy, -OC(=O)1-12C alkyl, -OC(=O)aryl, -OC(=O)N(R)2 or -OC(=O)OR7;

aryl = furyl, thienyl, pyrrolyl or pyridyl (all optionally substituted by one or two 1-4C alkyl) or -(CH2)f-phenyl in which f is 0-2 and the phenyl ring is optionally substituted by 1-3 Cl, Br, F, 1-3C alkyl, 1-3C alkoxy, 1-3C thioalkoxy, CCl3, CF3, NH2 or NHCOCH3;

R = H, 1-4C alkyl or phenyl;
R4 = H, CH3, Cl or F;
R5 = H, OH, F, Cl, Br, CH3, phenyl, vinyl or allyl;
R6 = H or CH3;
R9 = CH2CH2OR26, CH2CH2OC(=O)R27, H, OH, CH3, F, =CH2, CH2C(=O)OR28, OR26, O(C=O)R27 or O(C=O)CH2(C=O)OR26;
R10 = -C triple bond CH, -CH=CH2, halo, CN, N3, OR26, OC(=O)R27, H, OH, CH3 or R10 forms a second bond between positions C-16 and C-17;
R12 = H or forms a double bond with R1 or R14;
R13 = halo, OR26, OC(=O)R27, NH2, NHR26, NHC(=O)R27, N(R26)2, NC(=O)R27, N3, H, OH, =O, -O-P(=O)(OH)2 or O-C(=O)-(CH2)tCOOH;
R14 = H or forms double bond with R12;
R15 = H, =O or OH;
R23 = OH, O-C(=O)-R11, -OP(O)-(OH)2 or -O-C(=O)-(CH2)tCOOH, or
R23 + R10 = a cyclic phosphate;
R11 = -Y-(CH2)n-X-(CH2)m-SO3H, -Y'-(CH2)p-X'-(CH2)q-NR16NR17 or -Z-(CH2)rQ;
Y = a bond or -O-;
X, X' = bond, -CON(R18)-, -N(R18)CO-, -O-, -S-, -S(O)- or -S(O)2-;
R18 = H or 1-4C alkyl;
R16, R17 = 1-4C alkyl optionally substituted by one hydroxy or
NR16R17 = pyrrolidino, piperidino, morpholino, thiomorpholino, piperizino or N(1-4C lower alkyl)piperizino;
n = 4-9;
m, q = 1-5;
p = 2-9;
Z = a bond or -O-;
Q = -R19-CH2COOH, -CO-COOH or CON(R21)CH(R22)COOH;
R19 = -S-, -S(O)-, -S(O)2, -SO2N(R20)- or N(R20)SO2;
R20 = H or 1-4C alkyl, provided that the total number of C atoms in R20 and (CH2)r is not greater than 10;
R21 = H and
R22 = H, CH3, -CH2COOH, -CH2CH2COOH, -CH2OH, -CH2SH, -CH2CH2SCH3 or CH2Ph-OH, or
R21 = Me and
R22 = H, or
R21 + R22 = -CH-2CH2CH2-, or
-N(R21)CH(R22)COOH = -NHCH2CONHCH2COOH;
Ph-OH = hydroxyphenyl;
R24 = C, 1-2C double bond or O;
R25 = C(R15)CH2-R23, OH, OR26, OC(=O)R27, R26, COOH, C(=O)OR26, CHOHCH2OH, CHOHCH2OR26, CHOHCH2OC(=O)R27, CH2CH2OHCH2CH2OR26, CH2CH2OC(=O)R27, CH2CN, CH2N3, CH2NH2, CH2NHR26, CH2N(R26)2, CH2OH, CH2OR26, CH2O(C=O)R27, CH2O(P=O)(OH)2, CH2SC(=O)R27, CH2NC(=O)CHR28OR26, C(=O)CHR28OC(=O)R27, or
R10 + R25 = =C(R28)2;
R26 = 1-6C (alkyl, branched alkyl, cycloalkyl, haloalkyl, aralkyl or aryl);
R27 = R26 + OR26 and
R28 = H, 1-6C (alkyl, branched alkyl, cycloalkyl).
ACTIVITY - Ophthalmological; hypotensive.
MECHANISM OF ACTION - None given.
USE - Used for reducing IOP and controlling IOP spiking for treating glaucoma and ocular hypertension.
ADVANTAGE - The angiostatic agent provides effective, long lasting control of IOP and the other IOP lowering compound provides immediate control of a patient's elevated IOP and hence less IOP spiking. The two agents lower IOP provide the effect via differing mechanisms.
Dwg.0/0

FS CPI
FA AB; GI; DCN
MC CPI: B01-A02; B01-B01; B01-B02; B01-B03; B01-B04; B04-H03; B07-E03; B07-F01; B10-B03B; B14-F02B; B14-F02D; B14-N03

TECH UPTX: 20010328
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred composition: The angiostatic agent is e.g. 4,9(11)pregnadien-17-alpha,21-diol-3,20-dione-21-acetate. The other IOP lowering agent is betaxolol.
The composition comprises 4,9(11)pregnadien-17-alpha,21-diol-3,20-dione-21-acetate and timolol.

ABEX UPTX: 20010328
ADMINISTRATION - Administration is topical.

EXAMPLE - A composition was prepared comprising (in weight%): apraclonidine HCl (0.58), 5beta-pregnane-3alpha,11beta,17alpha,21 tetrol-20-one (tetrahydrocortisol) (1.0), Tyloxapol (0.01-0.05), hydroxypropylmethylcellulose (0.5), benzalkonium chloride (0.01), NaCl (0.8), edetate disodium (0.01), NaOH/HCl (to pH 7.4) and purified water (to 100 ml).

L76 ANSWER 6 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1999-405111 [34] WPIX
CR 1990-007032 [01]; 1990-253569 [33]; 1991-101860 [14]; 1993-182484 [22]; 1999-131871 [11]
DNC C1999-119586
TI Angiostatic agents and their compositions.
DC B01
IN CLARK, A F
PA (ALCO-N) ALCON LAB INC; (CLAR-I) CLARK A F
CYC 25
PI WO 9932127 A1 19990701 (199934)* EN 33 A61K031-57
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU BR CA JP MX
AU 9917142 A 19990712 (199950)
US 5990099 A 19991123 (200002) A61K031-58
EP 1039912 A1 20001004 (200050) EN A61K031-57
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
BR 9813684 A 20001010 (200055) A61K031-57
AU 734436 B 20010614 (200140) A61K031-57
MX 2000005276 A1 20010201 (200168) A61K031-56
JP 2001526233 W 20011218 (200203) 47 A61K045-00
EP 1039912 B1 20020807 (200259) EN A61K031-57
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
DE 69807115 E 20020912 (200268) A61K031-57
ES 2177112 T3 20021201 (200305) A61K031-57
ADT WO 9932127 A1 WO 1998-US25913 19981207; AU 9917142 A AU 1999-17142 19981207; US 5990099 A Cont of US 1988-264918 19881031, CIP of US 1989-419226 19891010, CIP of US 1990-559123 19900727, Cont of US 1992-941485 19920908, Cont of US 1994-349342 19941202, Cont of US 1996-643387 19960506, CIP of US 1997-990424 19971215, US 1997-994114 19971219; EP 1039912 A1 EP 1998-961956 19981207, WO 1998-US25913 19981207; BR 9813684 A BR 1998-13684 19981207, WO 1998-US25913 19981207; AU 734436 B AU 1999-17142 19981207; MX 2000005276 A1 MX 2000-5276 20000529; JP 2001526233 W WO 1998-US25913 19981207, JP 2000-525118 19981207; EP 1039912 B1 EP 1998-961956 19981207, WO 1998-US25913 19981207; DE 69807115 E DE 1998-607115 19981207, EP 1998-961956 19981207, WO 1998-US25913 19981207; ES 2177112 T3 EP 1998-961956 19981207
FDT AU 9917142 A Based on WO 9932127; US 5990099 A Cont of US 4876250, Cont of US 5371078, Cont of US 5698545; EP 1039912 A1 Based on WO 9932127; BR 9813684 A Based on WO 9932127; AU 734436 B Previous Publ. AU 9917142, Based on WO 9932127; JP 2001526233 W Based on WO 9932127; EP 1039912 B1 Based on WO 9932127; DE 69807115 E Based on EP 1039912, Based on WO 9932127; ES 2177112 T3 Based on EP 1039912
PRAI US 1997-994114 19971219; US 1988-264918 19881031;
US 1989-419226 19891010; US 1990-559123 19900727;
US 1992-941485 19920908; US 1994-349342 19941202;
US 1996-643387 19960506; US 1997-990424 19971215

IC ICM A61K031-56; A61K031-57; A61K031-58; A61K045-00
ICS A61K031-573; A61K031-575; A61P027-06; A61P043-00; C07J001-00; C07J003-00; C07J005-00; C07J013-00; C07J031-00; C07J041-00

AB WO 9932127 A UPAB: 20030121
NOVELTY - A new method for treating GLC1A glaucoma comprises administration of an angiostatic agent.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a composition for controlling GLC1A glaucoma comprising an angiostatic agent, preferably of formula (A) or (B).
ACTIVITY - Angiostatic.
MECHANISM OF ACTION - Inhibition of GLC1A gene expression.
USE - The method is useful for treating GLC1A glaucoma.
Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B01-A02; B01-A03; B01-D01; B01-D02; B14-N03

TECH UPTX: 19990825
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: The composition preferably contains 0.005 to 5%, especially 0.05 to 2%, of the angiostatic agent.
Preferred Drugs: The angiostatic agent is preferably of formula (A) or (B):
R1 = H, betab-CH3 or beta-C2H5;
R2 = F, C9-C11 double bond, C9-C11 epoxy, H or Cl;
R3 = H, OR26, OCOR27, halo, C9-C11 double bond, C9-C11 epoxy, =O, OH, 1-12C alkoxy, OCO(1-12C alkyl), OCOaryl, OCONR2 or OCOOR7;
aryl = furyl, thienyl, pyrrolyl or pyridyl (all optionally substituted by up to 2 of 1-4C alkyl) or -(CH2)f-phenyl (optionally substituted by up to 3 of Cl, F, Br, 1-3C alkyl, 1-3C alkoxy, 1-3C thioalkyl, CCl3, CF3, NH2 or NHCOCH3;
f = 0-2;
R = H, 1-4C alkyl or phenyl;
R7 = aryl or 1-12C alkyl;
R4 = H, CH3, Cl or F;
R5 = H, OH, F, Cl, Br, CH3, phenyl, vinyl or allyl;
R6 = H or CH3;
R9 = CH2CH2OR26, CH2CH2OCOR27, H, OH, CH2, F, =CH2, CH2COOR28, OR26, OCOR27 or OCOCH2COOR26;
R10 = -Cequivalent toCH, -CH=CH2, halo, CN, N3, OR26, OCOR27, H, OH, CH3 or a double bond between C-16 and C-17;
R12 = H or a double bond with R1 or R14;
R13 = halo, OR26, OCOR27, NH2, NHR26, NHCOR27, N(R26)2, NCOR27, N2, H, OH, =O, OPO(OH)2 or OCO(CH2)tCOOH;
t = 2-6;
R14 = H or a double bond with R12;
R15 = H, =O or OH;
R23 = OH, OCOR11, OPO(OH)2 or OCO(CH2)tCOOH or with R10 = cyclic phosphate;
R11 = -Y-(CH2)n-X-(CH2)mSO3H, -Y'-(CH2)p-X'-(CH2)q-NR16R17 or -Z(CH2)rQ;
Y = a bond or -O-;
Y' = a bond, -O- or -S-;
X, X' = a bond, CONR18, NR18CO, O, S, SO or SO2;
R18 = H or 1-4C alkyl;
R16, R17 = 1-4C alkyl optionally substituted by OH; or
R16-N-R17 = pyrrolidino, piperidino, morpholino, thiomorpholino, piperazino or N(1-4C alkyl)piperazino;
n = 4-9;
m = 1-5;
p = 2-9;
q = 1-5;
Z = a bond or O
r = 2-9;
Q = -R19CH2COOH, -COCOOH or CONR21CHR22COOH;

r = 2-9;
Q = R19 = S, SO, SO2, SO2NR20 or NR20SO2;
R20 = H or 1-4C alkyl provided that the number of C-atoms in R20 and (CH2)r is not greater than 10;
R21 = H; and
R22 = H, CH3, CH2COOH, CH2CH2COOH, CH2OH, CH2SH, CH2CH2SCH3 or CH2(4-hydroxyphenyl); or
R21 = CH3; and
R22 = H; or
R21+R22 = -CH2CH2CH2- ; or
NR21CHR22COOH = NHCH2CONHCH2COOH;
provided that if R23 is a phosphate it must form a cyclic phosphate, with R10 when R13 = =O, except for the compound in which
R1 = beta-CH3;
R2+R3 = C9-C11 double bond;
R4, R6 = H;
R12+R14 = C4-C5 double bond;
R5 = alpha-F;
R9 = beta-CH3;
R10 = alpha-OH;
R13, R15 = =O;
R23 = OPO(OH)2;
R24 = C, C1-C2 double bond or O;
R25 = CR15CH2R23, OH, OR26, OCOR27, R26, COOH, COOR26, CHOHCH2OH, CHOHCH2OR26, CHOHCH2OCOR27, CH2CH2OH, CH2CH2OR26, CH2CH2OCOR27, CH2CN, CH2N3, CH2NH2, CH2NHR26, CH2N(R26)2, CH2OH, CH2OR26, CH2OCOR27, CH2OPO(OH)2, CH2OPO(OR26)2, CH2SH, CH2SR26, CH2SCOR27, CH2NCOR27, COCHR28OH, COCHR28OR26, COCHR28OCOR27 or R25+R10 = =C(R28)2;
R26 = 1-6C alkyl, 3-6C cycloalkyl, 1-6C haloalkyl, aryl(1-6C alkyl) or aryl;
R27 = R26+OR26;
R28 = H, 1-6C alkyl or 3-6C cycloalkyl.
Most preferably the angiostatic agent is 4,9(11)-pregnadien-17alpha,21-diol-3,20-dione-21-acetate or 4,9(11)-pregnadien-17approximately,21-diol-3,20-dione.

ABEX UPTX: 19990825
EXAMPLE - A typical composition contains angiostatic steroid (0.005 - 5%), tyloxapol (0.01 - 0.05%), HPMC (0.5%), benzalkonium chloride (0.01%), sodium chloride (0.8%), edetate disodium (0.01%), NaOH/HCl (to pH 7.4) and water (to 100ml).

=> d his

(FILE 'HOME' ENTERED AT 16:07:03 ON 01 SEP 2004)
SET COST OFF

FILE 'REGISTRY' ENTERED AT 16:07:11 ON 01 SEP 2004
E ANECORTAVE/CN
L1 1 S E3,E4
SEL RN
L2 0 S E1/CRN

FILE 'HCAPLUS' ENTERED AT 16:08:35 ON 01 SEP 2004
L3 89 S L1
L4 10 S ANECORTAVE OR ANECORTAVE ACETATE OR NSC15475 OR NSC24345 OR N
L5 91 S L3,L4
L6 14 S L5 AND (EYE+OLD,NT,PFT,RT OR EYE, DISEASE+OLD,NT,PFT,RT)/CT
L7 9 S L5 AND EYE#/CW (L) DISEASE
L8 14 S L6,L7

FILE 'REGISTRY' ENTERED AT 16:11:26 ON 01 SEP 2004
L9 1 S 10184-70-0

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L10          0 S 10184-70-0/CRN

     FILE 'HCAPLUS' ENTERED AT 16:11:47 ON 01 SEP 2004
L11         45 S L9
L12          1 S AL4940 OR AL 4940
L13         45 S L11,L12
L14          8 S L13 AND (EYE+OLD,NT,PFT,RT OR EYE, DISEASE+OLD,NT,PFT,RT)/CT
L15          6 S L13 AND EYE#/CW (L) DISEASE
L16         16 S L8,L14,L15
L17        119 S L5,L13
L18          0 S L17 AND AMD
L19          3 S L17 AND MACUL? DEGENER?
L20          3 S L17 AND EYE, DISEASE/CT (L) (MACULA OR DEGEN? OR SENIL?)
L21         16 S L16,L19-L20
L22         13 S L21 NOT L19,L20
               E EYE+ALL/CT
L23     184018 S E26+OLD,NT,PFT,RT OR E27+OLD,NT,PFT,RT OR E28+OLD,NT,PFT,RT
L24         11 S L17 AND L23
L25          3 S L24 AND L19,L20
L26          8 S L24 NOT L25
L27         13 S L22,L26
L28          1 S US20040127472/PN OR (WO2003-US20154 OR US2002-401220#)/AP,PRN
               E JERDAN J/AU
L29          7 S E4-E6
               E ZILLIOX P/AU
L30          2 S E4
               E ROBERTSON S/AU
L31        151 S E3,E15,E16
               E ROBERTSON STELLA/AU
L32         20 S E3-E5
L33          2 S L17 AND L28-L32
               E ALCO/PA,CS
               E ALCOM/PA,CS
L34        877 S E3-E8 OR ALCON?/PA,CS
L35         12 S L17 AND L34
L36         19 S L19-L22,L27,L28,L35
L37         19 S L36 AND L3-L8,L11-L36
L38         18 S L37 AND (PD<=20020805 OR PRD<=20020805 OR AD<=20020805)
L39          2 S L19,L20 AND L38
L40          3 S L19,L20,L39
L41         16 S L37-L38 NOT L40
               SEL DN AN 15 16
L42         14 S L41 NOT E1-E6
L43          1 S L33,L35 NOT L40,L42
L44         16 S L41,L42

     FILE 'REGISTRY' ENTERED AT 16:23:44 ON 01 SEP 2004

     FILE 'HCAPLUS' ENTERED AT 16:23:57 ON 01 SEP 2004

     FILE 'EMBASE' ENTERED AT 16:25:24 ON 01 SEP 2004
L45         27 S L1 OR L9
L46         33 S L4 OR L12
L47         33 S L45,L46
               E EYE DISEASE/CT
L48         31 S E3+NT AND L47
               E EYE/CT
L49         10 S E3+NT AND L47
L50         32 S L48,L49
L51         23 S L47 AND MACUL?(L)DEGEN?
L52         23 S L50 AND L51
               E MACULA DEGENERATION/CT
               E E3+ALL
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L53         7817 S E2+NT
L54          244 S E4+NT
L55          250 S E6+NT
L56         2790 S E8+NT
L57           23 S L53-L56 AND L47
L58           23 S L52,L57
L59            6 S L58 AND PY<=2002
L60           10 S L47 NOT L58

     FILE 'EMBASE' ENTERED AT 16:29:04 ON 01 SEP 2004

     FILE 'MEDLINE' ENTERED AT 16:29:31 ON 01 SEP 2004
L61           12 S L47
                 E MACULA DEGENERATION/CT
                 E RETINA MACULA DEGENERATION/CT
                 E RETINAL MACULA DEGENERATION/CT
                 E EYE DISEASE/CT
                 E E5+ALL
                 E E208+ALL
L62        14366 S  E4+NT
L63            4 S L61 AND L62
L64            5 S L61 AND MACUL?(L)DEGEN?
L65            1 S L63,L64 AND PY<=2002

     FILE 'MEDLINE' ENTERED AT 16:31:53 ON 01 SEP 2004

     FILE 'BIOSIS' ENTERED AT 16:32:03 ON 01 SEP 2004
L66           29 S L47
L67           16 S L66 AND MACUL?(L)DEGEN?
L68            8 S L67 AND PY<=2002

     FILE 'BIOSIS' ENTERED AT 16:34:26 ON 01 SEP 2004

     FILE 'WPIX' ENTERED AT 16:34:36 ON 01 SEP 2004
L69            6 S L12/BIX OR L4/BIX
                 E ANECORTAVE/DCN
                 E ANECORTAVE/CN
L70            1 S E3
                 E RAOEF8/DCN
                 E RA0EF8/DCN
L71           11 S E3-E7
L72           12 S L69,L71
L73            5 S L72 AND (MACUL?(L)DEGEN?)/BIX
L74            2 S L72 AND (AMD OR ARMD)/BIX
L75            6 S L73,L74
L76            6 S L72 NOT L75

     FILE 'WPIX' ENTERED AT 16:37:51 ON 01 SEP 2004

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